

S E L E C T I V E S U R G E R Y
I N T H E
T R E A T M E N T O F D U O D E N A L U L C E R.

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P A R T I.

INTRODUCTION.

CHAPTER I.

Man, living in a constantly changing external milieu is persistently faced by an increasing host of maladies, primarily initiated by the stresses and strains imposed on him, in his struggle for survival in an ever changing physical and social climate.

Every phase of civilisation, has fostered its own crop of medical problems challenging human ingenuity. Our era characterised by its increased psychological burdens; fear, frustration, tension and lack of security ^{bring it} has posed duodenal ulceration as one of its most prominent problems.

Incidence:

Arriving at a true estimate of duodenal ulceration is virtually impossible. It has been shown that juxta-pyloric ulceration, including duodenal ulceration, affecting predominantly young and middle-aged men has increased twofold in the twenty years between the two world wars and that this trend is continuing since the last war (Jones and Gummer, 1961).

In 14,000 barium meal investigations done by Jennison (Jennison, 1938) in 1938 the incidence of duodenal ulceration was 7%. Ten years later in 20,000 barium meal investigations done by Feldman (Feldman, 1948) the incidence was 10%. In general hospitals in Britain the admission rate for duodenal

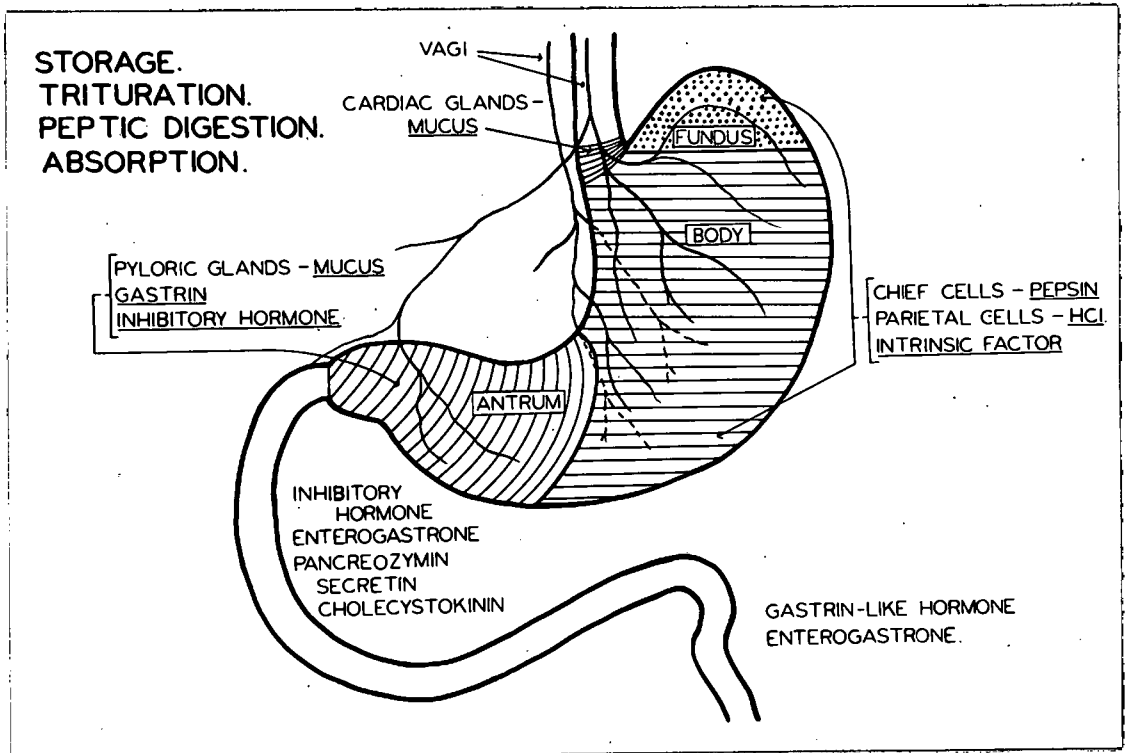


FIG. I.
DIAGRAM OF STOMACH.

x ulceration is about 8%. Of the general population, about 6% of men of working age and 2% of women are believed to suffer from peptic ulceration (Doll⁺/Jones, 1951). Of those admitted to hospital 2 out of 3 with peptic ulceration are duodenal in nature. One in 500 of the working population is treated for peptic ulcer each year and the average death rate from the disease is estimated to be 0.3% per year (Johnson, 1959). Each year 36000 operations for duodenal ulceration are performed in Britain, (Davey 1959). One in 20 of the population has lost most of his stomach before he dies.

In the United States of America approximately 2.5 million persons suffer from peptic ulceration, that is 15 per 1000 population.

Phsyiology:

While the basic derangements responsible for duodenal ulcer pathogenesis are not understood, it is generally accepted that the majority of cases are associated with increased hydrochloric acid secretion by the stomach, and therefore it is desirable to briefly review the present status of gastric secretory physiology.

The stomach (fig. I) a complex organ of which the function is not even fully understood today, embraces as its major functions:-

4/..... (i) Storage

- (i) Storage
- (ii) Motility
- (iii) Secretion
- (iv) Digestion
- (v) Absorption
- (vi) Sterilisation

The first major observations on gastric physiology were by William Beaumont (Beaumont, 1833) in 1825 on his remarkable subject Alexis St. Martin who had a gastric fistula due to a war wound. He could thus observe the changes in gastric secretion to various stimuli. No definite conclusions were drawn from this but he left it to subsequent workers to formulate their own interpretations.

Isolation of hydrochloric acid from gastric juice was first accomplished by Prout (Prout, 18⁸/24) in 1823, who showed that this was the specific acid concerned in gastric digestion.

Pepsin was isolated by Theodor Schwann (Schwann quoted by Portis, 1944) in 1835 as the enzyme of peptic digestion.

At the present stage of our knowledge gastric acid secretion is known to be dependent on three variables:-

- (i) Nervous
- (ii) Hormonal
- (iii) Parietal cell mass

Classically the physiological mechanism of gastric secretion was described in three phases:-

- (i) Cephalic phase (nervous, psychic).
- (ii) Gastric phase.
- (iii) Intestinal phase.

In the light of modern knowledge showing that there is a marked overlap of these phases it is perhaps better to assess the various components in their relation to gastric secretion. It has been recently suggested by Nyhus et al (Nyhus et al 1960) that a new ^{classification} terminology for the stimulatory phase of gastric secretion should be (i) direct vagal, (ii) vagal antral, (iii) local antral and (iv) intestinal.

A. The Role of the Vagus.

Brodie (Brodie, 1814) in 1814 demonstrated that section of the vagi suppressed gastric secretion in animals, but his views were not widely accepted. It remained for Pavlov (Pavlov, 1902) in 1889 in his classical experiments to establish beyond doubt the role of the vagi in gastric secretion. By "sham-feeding" experiments, using a dog with a cervical oesophagotomy and a gastric fistula, he proved beyond doubt that feeding produced a copious flow of highly acid gastric juice from the gastric fistula within 5 minutes. After section of the vagi with the animal feeding in the same way, no such flow occurred.

Working with the German physiologist Heidenhain in 1877, Pavlov learned the technique of constructing an isolated gastric pouch from the greater curvature of the stomach, maintaining the vagal innervation in contrast to the denervated Heidenhain pouch. The adequacy of this pouch was suspect for experimental purposes, because only a thin bridge of seromuscular coat remained between the stomach remnant and the isolated pouch, perhaps jeopardising the vagal integrity of the pouch.

It remained for Dragstedt (⁺Dragstedt, Ellis, 1930) to develop a technique of isolating the entire stomach of the dog preserving its entire vagal innervation. In this preparation the vagal phase of gastric secretion could now be studied and found to be much more prominent.

The nervous mechanism in man was first described in 1916 by Carlson (Carlson 1916) in a subject with a lye stricture of his oesophagus and a surgically created gastric fistula. He showed that by masticating palatable food a flow of gastric juice resulted. The nervous mechanism in humans can best be demonstrated by insulin induced hypoglycaemia. The latter is produced by giving intravenous crystalline insulin. The gastric secretory response occurs when the blood sugar falls to 50% or less of the fasting level. This response completely disappears after section of the vagi and thus forms the basis of the insulin test for the completeness of vagotomy.

In 1933, Stratten (~~Stratten~~, 1933) of Cologne noted that gastric secretion, excited by "sham-feeding" of dogs markedly decreased after resection of the pyloric region of the stomach, and thus postulated that for vagal stimulation of acid secretion to occur, at least a portion of the antrum must be present. Worobjew and Volborth (~~Worobjew~~, ~~Volborth~~, 1934) were unable to confirm these findings subsequently. This controversy of the influence of the vagus on the antrum lasted for 30 years. Uvnäs (~~Uvnäs~~, 1942) then presented the theory that the cephalic phase of gastric secretion is controlled by a combined neurohumoral mechanism and that the pyloric region played an important part in this mechanism. He concluded that a "secretagogue agent" was liberated from the pyloric region during vagal stimulation which in turn acted in an excitatory capacity to potentiate the direct effect of the vagus on the parietal cells. Clarification of this issue came with the report of Lim and Mozer (~~Lim~~, ~~Mozer~~, 1951) in 1951 that "sham-feeding" in oesophagostomised dogs with gastric fistula produced gastric secretory responses greater in amount and deviation than could be explained on the basis of the cephalic phase alone.

The two experimental techniques that really clarified this complicated problem were:

1. Production of a vagally innervated isolated antrum

x (Lim,⁺ Mozer, 1951; Woodward et al, 1952; Forrest, 1956; Oberhelman et al, 1957): In this experiment the innervated antrum is separated from the main stomach by a double mucosal bridge and the pyloric end is brought out to the skin as a fistula. Thus the antrum is removed from the rest of the stomach and also from duodenal influences and any changes in gastrin release, as reflected by the secretion in a Heidenhain pouch, must be due to vagal stimuli only. Forrest (Forrest, 1956) was the first to demonstrate this increased secretion in a Heidenhain pouch after isolation of the antrum. This was confirmed by Nyhus (Nyhus et al, 1960) who demonstrated that the release of gastrin from the antrum following vagal stimulation is a direct effect either via the vagus or via the intrinsic plexuses in the submucosa of the antrum. Woodward et al (Woodward et al, 1957) and Oberhelman et al (Oberhelman et al, 1957) clearly demonstrated the release of gastrin by insulin hypoglycaemia utilising the isolated innervated antral pouch and a Heidenhain indicator pouch.

x 2. The technique of antro-neurolysis (Lim,⁺ Mozer, 1950;

Jones et al, 1957): By this technique the antral submucosa is separated from the mucosa and interrupts intramural nerve connections from the vagus and ^{can} could be used to study further

facets of vagal gastrin release. Using this method in dogs
Chapman et al (Chapman et al, 1960) refuted a previous concept
that increased antral motility represented the prime mechanism
for release of gastrin by vagal stimulation and confirmed the
work of Thein and Schofield (Thein, Schofield, 1958) who
showed a lack of correlation between antral motility and acid
secretion from a transplanted fundic pouch.

The exact mechanism of gastrin release is unknown, but
regardless of this, it has now been shown that gastrin release
by vagal stimulation is entirely separable from that released
by local antral factors (Nyhus et al, 1960). That this phase of
acid secretion is important in the overall spectrum of gastric
secretion has been proved by de Vito et al (de Vito et al 1950)
who demonstrated that there is a 20-80% drop in a 24 hour
Heidenhain pouch secretion after antroneurolysis.

The reason for this marked reduction was then investigated
and it was shown that the responsiveness of the stomach mucosa was
markedly reduced after vagotomy (Antia et al, 1953; Code, 1953).
Kay (Kay, 1961) demonstrated that the withdrawal of tonic
cholinergic release at parietal cell level (vagal permissive
background) plays a major role in the reduction of maximal acid
secretory capacity which follows vagotomy. It may be stated that
the vagus nerves apparently have a background effect on the

secretory mechanism of the mucosa acting as a sensitiser of gastric secretion so that when secretory stimuli reach the mucosa the response is more prompt and effective. After vagotomy the mucosa is more sluggish to some forms of stimulation.

These experiments have proven that the vagus controls gastric acid secretion by 3 mechanisms:

(i) Cephalic phase of gastric secretion
(Pavlov, 1902).

(ii) Effect of the vagus on the antral phase of gastric secretion with resultant gastrin production. (Uvnäs 1942; Lim⁺, Mozer 1951; Woodward et al 1957; Forrest 1956; Oberhelman et al 1957; Nyhus et al 1960; Lim⁺, Mozer 1950; Jones et al 1957; Chapman et al 1960; Thein⁺, Schofield 1958; de Vito et al 1950; Antia et al 1953; Code 1953; Kay 1961).

3. Vagal permissive background (Kay 1961).

Knowing that the vast majority of patients with duodenal ulceration suffer from gastric hypersecretion the obvious question therefore arises - Is there specific vagal hyperactivity present in duodenal ulceration?

At this stage of our knowledge this is indeed a difficult question to settle. Dragstedt (~~Dragstedt~~ 1951) is one of the foremost protagonists of specific vagal hyperactivity in duodenal

ulceration. He believes that patients with duodenal ulceration secrete excessive amounts of gastric juice more or less continuously and that this secretion is dependent on vagal control.

Conversely this theory is disputed by Hunt, Kay and others (Hunt⁺, Kay 1959; Bruce et al 1959) who have shown that there is no need to postulate the existence of such a supranormal activity, as the percentage diminution in nocturnal secretion following vagotomy was of the same order in gastric ulcer subjects as in those with duodenal ulcers.

It thus appears from this work that specific vagal hyperactivity cannot be accepted as the cause of gastric hypersecretion in patients with duodenal ulceration. It is well known however, that vagotomy alone will reduce acid secretion by 20-80% of basal or histamine stimulated output. This suggests therefore, that the vagus has a centrally or permissive effect on all acid secretion and it is possible that acetylcholine constitutes the final chemical stimulus for acid secretion at the parietal cell level (Grossman 1961) despite the generally held view that histamine appears to be the final common stimulus.

Finally it must be stressed that the vagus plays an outstanding role in the therapy of duodenal ulceration. Irrespective of how attractive the hypothesis of specific vagal hyperactivity

in this disease may seem, it cannot as such be accepted.

B. The Role of the Gastric Antrum.

x As early as 1906, ~~Edkins~~ (Edkins, 1906) demonstrated that the antral mucosa contained a "substance which produced copious acid secretion if extracts of antral mucosa was injected intravenously." He called this substance "gastrin" and postulated the "gastrin theory" of gastric acid secretion. This work was not accepted on technical grounds and was thus disregarded for many years. Further proof of this theory was delayed until 1925 when Ivy and Farrell (~~Ivy, Farrell~~, 1925) successfully transplanted a fundic gastric pouch into the mammary region of the dog, leaving the antrum in situ. If this animal was fed the transplanted pouch secreted a minute but quite definite amount of acid. It was then accepted for the first time that a humoral agent capable of stimulating gastric acid secretion was circulating in the blood stream after a meal. Striking confirmation of this work was produced by Feng, Hou and Lim (~~Feng et al~~, 1929) in 1929, who, using denervated and transplanted fundic pouches for another purpose, obtained prompt and considerable responses to feeding a meal of meat, leaving no doubt that a humoral stimulant of gastric secretion appeared in the circulation soon after feeding a conscious dog.

xx
x
In 1938 Komarov (~~Komarov~~, 1938) isolated a hormone from the protein fraction of gastric juice. As other workers could not successfully repeat Komarov's work it was thought that the gastric stimulation might be due to histamine, despite the ^{claim} fact that Komarov's preparation was ~~reputedly~~ histamine free. The nature and origin of gastrin was determined by Ivy and Gregory (~~Gregory~~, Ivy, 1941) and the term "gastrin", originally coined by Edkins, was finally accepted. That this hormone was released by the antral mucosa in response to antral distension, or the local action of secretagogue or chemical stimuli on the stomach, appeared to have been confirmed. (Lim et al, 1925).

x
More recently it has been shown that gastrin also influences the reactivity of the parietal cell mass to other stimuli. It was shown by ~~Stavney~~ (^{by} Stavney et al, 1962) that administration of a very small dose of gastrin which of itself causes very little secretion of acid from a denervated pouch, is sufficient to increase markedly the response to a moderate dose of histamine.

x
Sokolov (~~Sokolov~~, cited ^{by} Babcock, 1950) demonstrated that the introduction of 0.5% hydrochloric acid into the stomach diminished the secretion from a Pavlov pouch. Other studies followed and showed that any procedure which will reduce or

neutralise gastric acidity such as vagotomy or gastro-jejunostomy will regularly result in excessive release of gastrin (Evans et al 1953; Zubiran et al 1952; Kanar et al 1952). If an isolated antral pouch is perfused with a solution of pH of 1.2 there is no augmentation of secretion from a Heidenhain indicator pouch indicating suppression of the gastrin mechanism (Woodward et al 1954;⁺ Woodward et al 1957). If this perfusate has a pH of 1.7 suppression will be ineffective, (Woodward et al 1957). Therefore the gastric content can be considered to constitute an autoregulatory mechanism. When the pH falls to about 1.5 the gastric phase of secretion is terminated (Gillespie, 1959) suggesting that the low pH was the basis of the physiologic cut-off mechanism. The mechanism by which acid inhibits the antral phase of gastric secretion remains a subject of some controversy. The experimental work of Harrison et al (Harrison et al, 1956) and Jordan and Sand (Jordan and Sand 1957) suggested the possibility of the antrum secreting an antisecretory hormone (antrogastrone). Other workers failed to repeat these studies with success (Johnson et al 1960; Longhi et al 1957; Woodward et al 1958; Shapiro et al 1960). Recent work done by Du Val and Price (Du Val, Price 1960) and by Lerner and Thompson (Thompson, Lerner 1961) further support the concept that the antrum does

produce an antiseecretory hormone.

At the present stage of our knowledge then, it remains very much an open question whether antral inhibition is a cut-off mechanism or whether it is due to an antiseecretory hormone or a combination of these 2 mechanisms.

From these studies it is obvious that the gastric antrum plays a major role in the control of gastric acid secretion in 2 ways and possibly a third:

(i) Acid stimulation (Woodward et al 1957).

(ii) Acid inhibition (Woodward et al 1954).

(iii) Antiseecretory hormone - antrogastrone

(Harrison et al 1956; Jordan⁺, Sand 1957; Du Val, Price 1960; Thompson⁺, Lerner 1961).

Knowing that the majority of duodenal ulcer patients secrete more acid than controls and knowing that there is unlikely to be specific vagal hyperactivity (Hunt⁺, Kay, 1959; Bruce et al, 1959) the question arises - Is there any evidence that gastrin hypersecretion occurs in patients with duodenal ulceration?

The only work to date on this aspect is that of Blair et al (Blair et al (1962) who demonstrated that the mucosa of the pyloric gland area in duodenal ulcer cases contain 2-3 times more gastrin than in gastric ulcer patients and controls.

^{T also}
~~Also~~ that there is no significant difference between concentrations of gastrin in the pyloric antra in patients with gastric ulcer and controls.

Although this work requires to be repeated it does seem that patients with duodenal ulceration have a higher level of antral gastrin when compared with gastric ulcer cases or controls.

C. The Role of the Parietal Cell Mass.

Anatomically the human stomach (fig. I is divided into:

- (i) The cardiac region.
- (ii) The fundus or fornix.
- (iii) The corpus or body.
- (iv) The pyloric vestibule.
- (v) The pyloric canal.

The first 3 of these divisions are often described together as the cardiac part of the stomach and the latter two as the pyloric part or antrum.

Physiologically the stomach can be divided into 2 parts:

(i) that part that secretes acid and pepsin and (ii) those parts which do not. The former is known as the fundus and is comprised of most of the corpus and the fundus of the stomach. The latter comprise the cardiac and pyloric regions. The cardiac area contains cardiac glands and extends as a narrow collar about a centimetre deep around the oesophageal opening. The

pyloric region or antrum occupies a greater length on the lesser than on the greater curvature of the stomach. According to the measurements to Erik Landboe-Christensen, the antrum occupies 44% of the distal portion of the stomach along the lesser curvature and approximately 12% along the distal greater curvature.

× The fundus and body of the stomach lying between the antrum and ^{cardiac} pyloric parts contain that section of the gastric mucosa carrying the glands containing the parietal cells which are responsible for the secretion of hydrochloric acid. The proof that these cells secrete hydrochloric acid was produced by ×× Linderström-Lang (Linderström-Lang et al (1934)). By cutting × parallel serial sections ^{they} he was able to correlate a low pH with a high parietal cell count. It has also been shown that the parietal cells are more densely distributed in the body of the stomach than in the fundic portion, but on the whole a fairly uniform distribution of parietal cells are present (Berger, 1934; Card and Marks, 1960).

It has been demonstrated that the total number of parietal cells in the gastric mucosa generally referred to as the parietal cell mass (P.C.M.) is directly responsible for the magnitude of gastric acid secretion in each individual. Guiss and Stewart (Guiss and Stewart, 1948) reported a significant

correlation between the highest concentration of acid reached during a fractional test meal and parietal cell counts of the subsequently resected stomachs. Tongen (Tongen(1950) showed that the total acid concentration attained during a triple histamine test (0.5 mg. histamine given subcutaneously at $\frac{1}{2}$ -hourly intervals for 3 doses) was roughly proportional to parietal cell concentrations per unit area of gastric mucosa. Marks et al (Marks et al(1960) have also found that maximal acid secretion following histamine stimulation was a linear function of both the total number of parietal cells and the fundic mucosal volume in dogs.

The observation that duodenal ulcer patients have a greater number of parietal cells than those with gastric ulcer-
ation was demonstrated by Meyers, (Meyers, 1923). Card and
Marks (Card, Marks(1960) showed that there is a quantitative
relationship between the total number of parietal cells and
maximal acid secretion of the stomach following histamine
stimulation in patients suffering from duodenal ulcers. Not
only is there an increased P.C.M. in these cases but also a
larger stomach and a bigger mucosal volume (Wangensteen et al
1940; Cox 1952). From the data quoted above it may be
confidently stated that the majority of patients suffering from

duodenal ulceration have a bigger parietal cell mass and thus will secrete a larger volume of hydrochloric acid than controls or those suffering from gastric ulceration.

D. The role of the duodenum and small intestine.

This phase of gastric secretion is probably not very important in man.

< Gregory and Ivy (Gregory, Ivy (1941), completely bypassed the stomach by anastomosing the oesophagus to the small intestine in dogs and showed that by direct feeding into the intestine, secretion in a Heidenhain as well as in a transplanted gastric pouch could be produced proving that this secretion was humoral in nature. That this secretion was caused by a hormone analogous to gastrin was shown by Sircus (Sircus 1953). He also showed that distension of the intestine in the same preparation will cause secretion in a Heidenhain pouch.

The inhibitory effect of duodenal acidification on gastric secretion has been widely confirmed. (Andersson 1960; Code 1951; Dragstedt 1957; Griffiths 1936; Jones Harkins 1959; Munch-Petersen et al 1944; Pincus et al 1942; Sircus 1958.) It was shown that this inhibitory mechanism is related to the concentration of acid and is not operative until the duodenal pH is 2.5 or less (Jones, Harkins 1959; Pincus et al, 1942). A

highly acid duodenal content will also inhibit gastric motility via the enterogastric reflex mediated through the splanchnic nerves. Sircus (Sircus 1958) showed that introducing hyperosmolar solutions into the duodenum leads to inhibition of gastric secretion and is hormonally mediated. Similarly gastric motility and secretion are inhibited by the presence of oil or fat in the duodenum mediated through the hormone enterogastrone (Grossman 1950). It is not known whether enterogastrone and the hormone functioning in duodenal hyperosmolar inhibition are the same. This aspect is under investigation at the moment.

Finally it can be stated that the clinical significance of duodenal inhibition on gastric secretion is impossible to assay. It was suggested by Shay, Gershon-Cohen and Fels (Shay et al, 1942) that patients with duodenal ulcer may be unusually resistant to the inhibitory effects of acid in the duodenum and this may partially explain the high levels of spontaneous acid secretion seen in these individuals.

Evolution of the Augmented Histamine Test.

Recognition of the P.C.M. in determining the magnitude of the acid secretory response of an individual (Guiss⁺, Stewart 1948; Tongen 1950; Meyers 1923; Cox 1952) emphasized the need for a reliable method of assessing the P.C.M. The stimulant

effect of histamine on gastric secretion has been known since 1920 (Popielski, 1920; Carnot et al 1922). Indeed histamine has been suggested by Babkin (Babkin 1950) to be the final common pathway of all gastric secretory stimuli.

x Adam et al (Adam et al (1954)) showed that increasing doses of histamine given intravenously produced an increased acid output and tended to a limiting value, which they suggested ^{might} ~~may~~ bear a definite relation to the P.C.M. A more practicable method for determining this limiting value was made possible by the observation that parenteral antihistaminics antagonise the unpleasant side effects of large doses of histamine without influencing its action on the stomach (Halpern 1947). This facilitated measurement of the acid secretory responses to graded doses of histamine, administered subcutaneously, in a large number of subjects (Conard et al 1949; Kay 1953) and the smallest dose of histamine acid phosphate found necessary to effect the maximal acid secretory response was established as 0.04 mg. per kg. of body weight (Kay 1953; Murray et al 1957).

/ The augmented histamine test, based on the latter dosage of histamine administered under antihistaminic cover, was popularised by Kay (Kay-1953) in 1953 and has since gained widespread acceptance as a routine test of gastric secretion of acid. Tests repeated in the same individual have given

remarkably consistent results (Kay, 1953; Marks and Shay unpublished data ¹⁹⁵⁹ 1960; Sircus 1960).

The demonstration of an excellent correlation between the acid output following maximal histamine stimulation and the parietal cell mass in both human subjects (Card ^{and} Marks 1960) and the dog (Marks et al 1960) indicates that the augmented histamine test provides the most satisfactory clinical measure of parietal cell mass presently available.

The technique of the augmented histamine test is simple, (Part II, (Chapter I). After aspiration of the fasting contents, the secretion collected over the next hour represents the basal secretion (basal acid output - B.A.O.) Following histamine stimulation the secretion collected over the following hour represents the maximal acid secretion (Maximal acid output - M.A.O.) that any individual is capable of producing.

Role of the Augmented Histamine Test in elucidation of the Pathophysiology of Duodenal Ulcer:

Our knowledge of the association of duodenal ulceration with gastric hypersecretion must unquestionably influence our understanding of the pathogenesis of this disease. It is also reasonable to accept that the acid secretory response depends on the 3 variables as previously stated - (i) nervous, (ii) hormonal and (iii) P.C.M.

The M.A.O. being a direct reflection of the P.C.M. (Card and Marks 1960; Marks et al 1960) and that the former is on the average twice as great as in controls (Shay 1959) - it is probable that a large P.C.M. is an important but not the sole determining factor in the pathogenesis of duodenal ulceration.

The same correlation of M.A.O. to P.C.M. can be proved by presenting experimental data in a somewhat different fashion.

Table I shows the relationship between the P.C.M. and the M.A.O. in controls and duodenal ulcer patients. In the controls the P.C.M. in billions was 0.98 and the M.A.O. 20.19 mEq HCl per hour (mEq/hr) whereas in duodenal ulceration the P.C.M. was 1.77 billion and the M.A.O. 35.74 mEq HCl per hour. Dividing the M.A.O. by the number of parietal cells a constant M.A.O. per billion parietal cells was obtained, proving the relationship between the M.A.O. and P.C.M. in the same individual.

It would then once again appear that the larger P.C.M. in duodenal ulcer cases account for the greater M.A.O. in such subjects.

That this increased P.C.M. in duodenal ulceration may be an important but not the sole determining factor in the pathogenesis of this disease is proved firstly by the fact that some controls have a greater mean P.C.M. than duodenal ulcer cases (Cox 1952)

RELATIONSHIP OF Parietal Cell Count IN
BILLIONS TO MAXIMAL ACID OUTPUT.

(Data derived from comparable
groups and the same individuals.)

M.A.O. / P.C.M.

<u>GROUP.</u>	<u>P.C.M.</u> (Billions i.e. 10^9)	<u>M.A.O.</u> <u>mEq HCl/hr.</u>	<u>M.A.O. in mEq/hr.</u> <u>per billion</u> <u>(par. cells)</u>
---------------	--	-------------------------------------	---

Control (C)	0.98 (107)	20.19 (105)	20.6
Duod. Ulcer. excl. DU:GU	1.77 (23)	35.74 (474)	20.2
References.	Cox 1952, 1957 Card, ^{and} Marks 1960	Marks, ^{and} Shay 1959 Sircus 1959, 1960 Kay, 1953.	

TABLE I.

Estimated average acid output following maximal histamine stimulation per billion (10^9) parietal cells. (Note that the larger P.C.M. in duodenal ulcer subjects would appear to account for the greater M.A.O.) Number in patients in parenthesis.

and secondly, the P.C.M. in dogs may be as great and even greater than the mean P.C.M. in duodenal ulcer subjects, yet never develop spontaneous duodenal ulceration (Marks, et al 1960).

No such correlation between the basal secretion and the P.C.M. can be obtained. A marked correlation does exist between the one hour basal secretion and the M.A.O. but this shows that only 30-50% of the variations can be explained by this correlation (Marks, ^{and} Shay unpublished data ¹⁹⁵⁹ 1960).

Presenting this data in a similar way as for the M.A.O.

(Table I) no similar constant relationship could be found.

Table II shows that the relationship between the B.A.O. and the P.C.M. differed in controls and patients with duodenal ulceration. In controls the B.A.O. per billion parietal cells was 2.2 mEq/hr. or 18.47 mEq/12 hour nocturnal secretion. On the other hand the B.A.O. per billion parietal cells in duodenal ulcer was 3.1 mEq/hr. and 34.69 mEq/12 hour nocturnal secretion showing that in duodenal ulcer the 12 hour nocturnal secretion per billion parietal cells to be nearly twice that in controls. This then shows that the basal secretion reflects not only the P.C.M. (Marks and Shay, unpublished data ¹⁹⁵⁹) but also vagal integrity and humoral stimulation of the parietal cells.

RELATIONSHIP OF Parietal Cell Count in Billions to Basal Secretion.

(Data derived from comparable groups and the same patient^s.)

B.A.O./P.C.M.

GROUP	P.C.M.	B.A.O. mEq/hr.	BAO/hr./10 ⁹	12 hr. noct. secre. in mEq.	12 hr. noct. Secr./10 ⁹	24 hr. basal in mEq.	24 hr. basal secre./10 ⁹
CONTROL (C)	0.98 (107)	2.18 (78)	2.2	18.1	18.47	52.1	53.2
DUODENAL ULCER.	1.77 (23)	5.40 (322)	3.1	61.4	34.69	110.1	62.2
REFERENCES.	Cox 1952 1957 Card Marks 1960	Sircus 1959 Marks + Shay 1959		Levin et al 1952		Levin et al 1952	

TABLE II.

Estimated average output of basal secretion in mEq per billion parietal cells in controls and duodenal ulcer patients. (Note there is no true relationship between basal secretion and P.C.M.) Number of patients in parenthesis.

There is little doubt regarding the importance of vagal integrity in the maintenance of gastric acid secretion in man, irrespective of how attractive the unproven (Bruce et al 1959) concept of specific vagal hyperactivity in duodenal ulcer is (Winkelstein 1942; Levin et al 1949; Dragstedt et al 1950). It is accepted by everybody today that a vagotomy regularly reduces acid output by about 65% (Gillespie and Kay 1961; Gillespie et al 1960; Falconer 1959; Gelb et al 1961) in the vast majority of patients but in a small proportion (10%) this reduction is only in the region of 20-30%. It was shown that in this latter group the hormonal phase of gastric secretion predominates and in the former the vagus is the predominant factor (Kay, 1961), and that the cases with hormonal preponderance can be ascertained pre-operatively by performing a "medical-vagotomy" as described by Smith and Kay (Smith, Kay (1956).

The possible role of hormonal overactivity in acid hypersecretion and in the pathogenesis of peptic ulceration, suggested by the experiments of Dragstedt (Dragstedt (1952) has been highlighted by the elucidation of the pathophysiology of the Zollinger-Ellison Syndrome (Marks et al 1961, Grossman et al 1961 and Gregory et al 1960).

In conclusion then it is reasonable to accept that the 3

factors which are important in gastric acid secretion are (i) nervous; (ii) hormonal; (iii) parietal cell mass. (Table III).

From the above discussion it is reasonable to accept that (i) the P.C.M. is directly responsible for the M.A.O. obtained in any individual, that (ii) the basal secretion reflects all three factors in varying degrees in different patients and that (iii) the augmented histamine test would appear to be the best laboratory method available today for assessing these variables (Table IV).

TABLE III.

FACTORS RESPONSIBLE FOR HYPERACIDITY
IN DUODENAL ULCERATION.

- | |
|--|
| 1. Increased parietal cell mass - mean 1.8×10^9 |
| 2. Vagal activity. |
| 3. Hormonal activity: antral gastrin
pancreatic gastrin
other endocrines |

TABLE IV.

THE AUGMENTED HISTAMINE TEST.

BASAL SECRETION	MAXIMAL ACID OUTPUT (MAO)
Parietal cell mass	Parietal cell mass
Vagal activity	
Gastrin release	

CHAPTER II.

THE EVOLUTION OF GASTRIC SURGERY.

Surgery of the stomach was initiated in the latter part of the last century in an attempt to relieve obstruction caused by carcinoma of the stomach. In due time it was applied to the therapy of peptic ulceration.

Throughout the years many factors have from time to time influenced surgeons in their choice of operative procedure. Three twenty-year periods emerged.

In the first 20 years of this century the surgeon was limited in the time at his disposal by the prodigious mortality rate and crude anaesthesia and therefore had to resort to quick simple procedures like gastroenterostomy. When the results of this period were evaluated, the alarming stomal ulcer incidence led to the adoption of more radical procedures, over the next 20 years. A further factor encouraging this, was the steadily declining mortality rate. During the third 20 year period, postgastrectomy side effects caused great concern, forcing reconsideration of the entire problem. With better understanding of gastric physiology, a new era of physiological surgery was introduced and with it a swing back to more simple procedures.

To-day it is accepted by all that no single operation will suit every patient with duodenal ulceration and therefore a variety of procedures have been evolved that are now in

current use (Fig. II). This change in surgical approach is adequately demonstrated by Fig. III showing the incidence of various procedures in Cape Town for the periods 1950-1959 and 1960-1963.

Gastric Resection:

Professor Theodor Billroth can rightly be called the father of gastric surgery. His thoughts and views, propagated by, and improved on by diligent pupils, laid the foundations on which we are still building to-day.

Billroth performed the first partial gastrectomy in 1881 for pyloric carcinoma. In 1885, Von Hacker (~~Von-Hacker~~ 1885) reported an operation done by Billroth which was to become known as the Billroth II gastrectomy. Few alterations were added to the Billroth I and Billroth II operations until the turn of the century. Although the danger of leakage from the anastomotic line in a Billroth I gastrectomy was very real, nevertheless it was persisted with in place of the safer Billroth II procedure, because many workers believed that exclusion of the duodenum would result in atrophy of the pancreas. (Burdenko, 1914).

Schoemaker in 1911 introduced his method of making the Billroth I procedure safe (Schoemaker 1911).

Stumpf (Stumpf (1908) in 1908 described the use of the

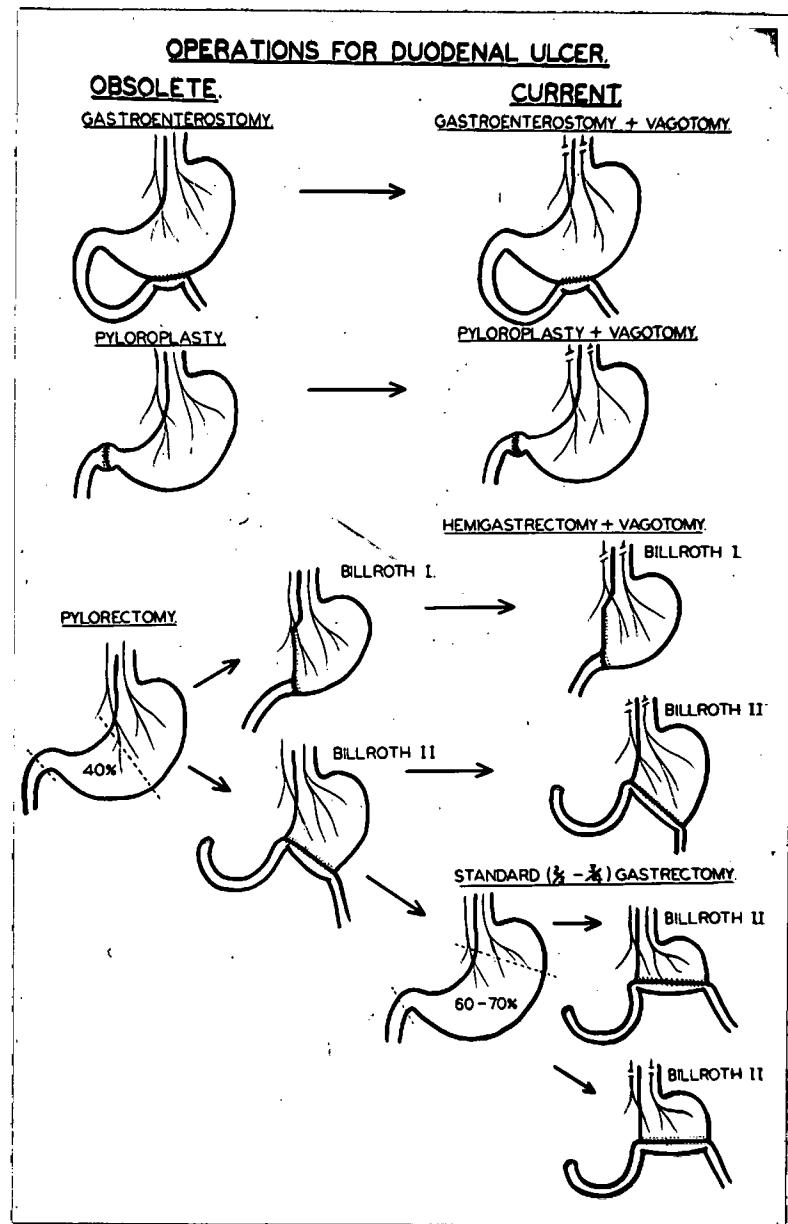


FIG. II.

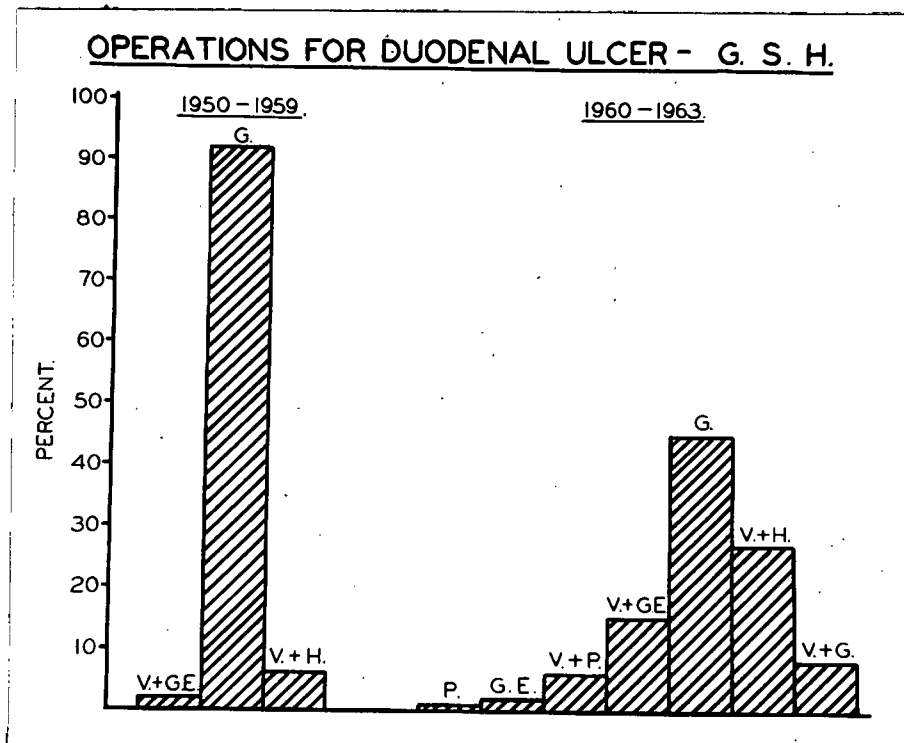


FIG. III.

Change in surgical approach to duodenal ulceration.

valved anastomosis which is ascribed to the work of Hofmeister. Finsterer (Finsterer 1923) reported that Hofmeister had used it as early as 1908.

Balfour, introducing the long anterior afferent loop in the Billroth II gastrectomy, soon met with difficulties due to retention of pancreatic and biliary secretions, which forced him to add an entero-anastomosis (Balfour 1925).

Following the introduction of partial gastrectomy into the treatment of duodenal ulceration, surgeons soon encountered the problem of the difficult ulcer penetrating into the pancreas. Antral exclusion technique became the fashion in these cases, only to be followed by a very high incidence of gastro-jejunal ulceration. To prevent this complication many modifications were tried (Devine 1925) without success. X Bancroft in 1932 (~~Bancroft~~ 1932) described his technique of coring out the antrum in an attempt to deal with this problem. Finsterer described the manoeuvre that is to-day known as the Bancroft manoeuvre (antral exclusion, partial gastrectomy and coring out the antrum) with a further decrease in gastro-jejunal ulceration. Roscoe Graham advocated exteriorization of the ulcer (Roscoe Graham, 1938) when the stump was difficult to close or when such closure was suspect and Welch later on introduced catheter

duodenostomy with or without catheter jejunostomy in similar cases (Welch 1949).

Throughout the years many modifications of partial gastrectomy were introduced (Moynihan 1928, Connell 1929, Wangensteen 1940, 1952) (Fig. IV). To-day the standard Billroth I and Polya gastrectomy techniques are well documented. Most surgeons prefer an antecolic anastomosis with a Hofmeister valve, although some dispense with the valve and others favour a retrocolic anastomosis. Orr recently described his retrocolic no-loop anastomosis at the duodeno-jejunal junction (Orr 1963). Reintroduction of vagotomy led to its use in addition to gastrectomy, the amount of stomach resected e.g. hemigastrectomy, antrectomy or Standard 2/3 resection, depending on the indications.

Gastroenterostomy.

It is believed that Von Rydygier performed the first gastroenterostomy for a known duodenal ulcer in 1880, with fatal results (Von Rydygier 1880). Woelfler claimed the first survivor following this procedure in 1881 (Woelfler 1881). The same worker performed the first anastomosis en-Y (Woelfler 1883) which was later popularised by Roux (Roux 1897).

The first retrocolic posterior gastroenterostomy was performed by Courvoisier (Courvoisier 1897). Petersen of

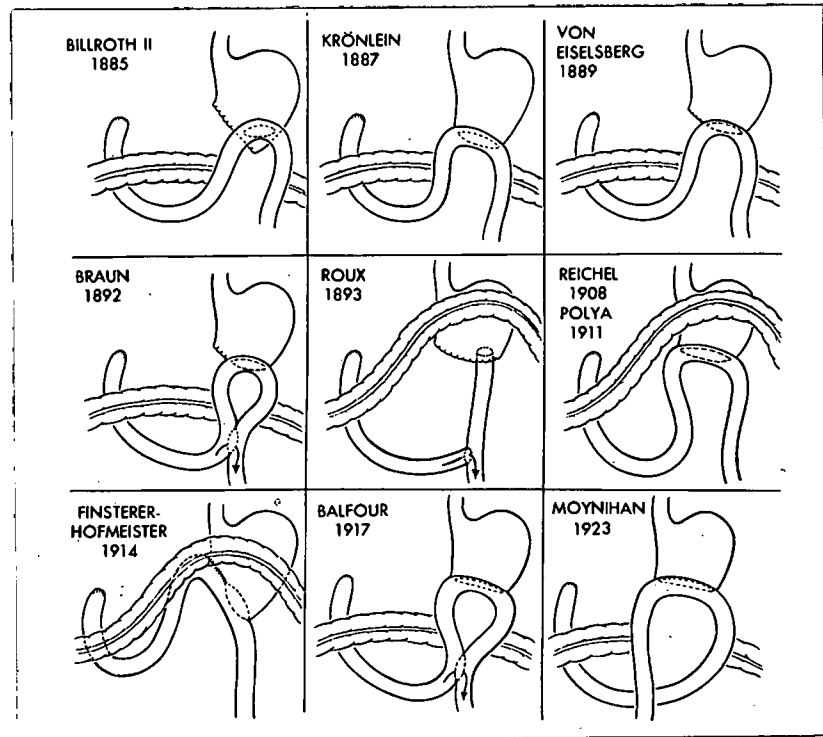


FIG. IV.

Past modifications of partial gastrectomy.

Germany overcame the major problems of this procedure, and laid the foundations of this manoeuvre as we know it to-day (Petersen 1901).

During the period 1900-1935 gastroenterostomy remained the procedure of choice for the surgical treatment of duodenal ulceration, but as early as 1913, Sir Arthur Hurst (Hertz 1913) published an article on the unfavourable aspects of the operation. It was slowly losing its popularity on the Continent in the 1920's because of the high recurrence rate of secondary ulceration, but British and American surgeons still favoured it as the procedure of choice. Their attitude was doubtless further prolonged because Sherren, in 1925, stated that absence of recurrent ulceration after 2-3 years constituted a cure (Sherren 1925). In 1929 Luff showed that this period of follow up was obviously too short because 68% of recurrent ulceration will only manifest after a period of 2-6 years. It is interesting to note that this period is twice as long following gastro-jejunostomy as compared with gastrectomy (Priestley, Gibson 1948, Edwards et al 1956, Walters et al 1955, Everson, Allan 1955, Everson, Allan 1955, Thompson 1956). The first jejunal ulcer was described in 1899 by Braun (Braun 1899).

To-day gastroenterostomy alone is rarely practised

except in the exceptional case with special indications.
On the other hand gastroenterostomy plus vagotomy is very popular in some centres. Usually a posterior short loop gastroenterostomy is performed, but a variation used by Tanner is his so-called anterior juxta-pyloric gastrojejunostomy (Tanner⁽¹⁹⁶³⁾).

Pyloroplasty:

The first workers to attempt this procedure were Heinecke in 1885 (Heinecke 1886) and Mikulicz in 1888 (Mikulicz - Radecki 1888). Finney described his method in 1926 (Finney 1926). When pyloroplasty is performed nowadays it is always associated with a vagotomy, the method of choice being a personal preference.

In Cape Town the Heinecke - Mikulicz variety is almost exclusively used.

Vagotomy:

A new era in peptic ulcer surgery was initiated in 1945 by Dragstedt and Owens when they introduced vagotomy as a method of treatment of duodenal ulceration (Dragstedt, ^{and} Owens 1943). This, however, was not new for it had been practised during the period 1900-1920 (Exener 1911, Bircher 1920, Latarjet 1922). Vagotomy alone soon proved to be inadequate because of unpleasant distension, eructation of foul smelling

gases and gastric ulceration. The addition of a drainage procedure overcame these difficulties so that to-day vagotomy is associated either with gastric resection or else a drainage procedure. Despite this, vagotomy still has its sequelae and a new trend recently has been selective vagotomy (Burge 1960).

Current Procedures. (Fig. V).

x It can be finally states^d then that the current manoeuvres practised in the surgery of duodenal ulceration are:

- (i) Drainage (gastroenterostomy or pyloroplasty) plus vagotomy.
- (ii) Standard 2/3 Polya gastrectomy.
- (iii) Hemigastrectomy, antrectomy with gastroduodenal or gastrojejunal anastomosis plus vagotomy.
- (iv) Standard Polya gastrectomy plus vagotomy.

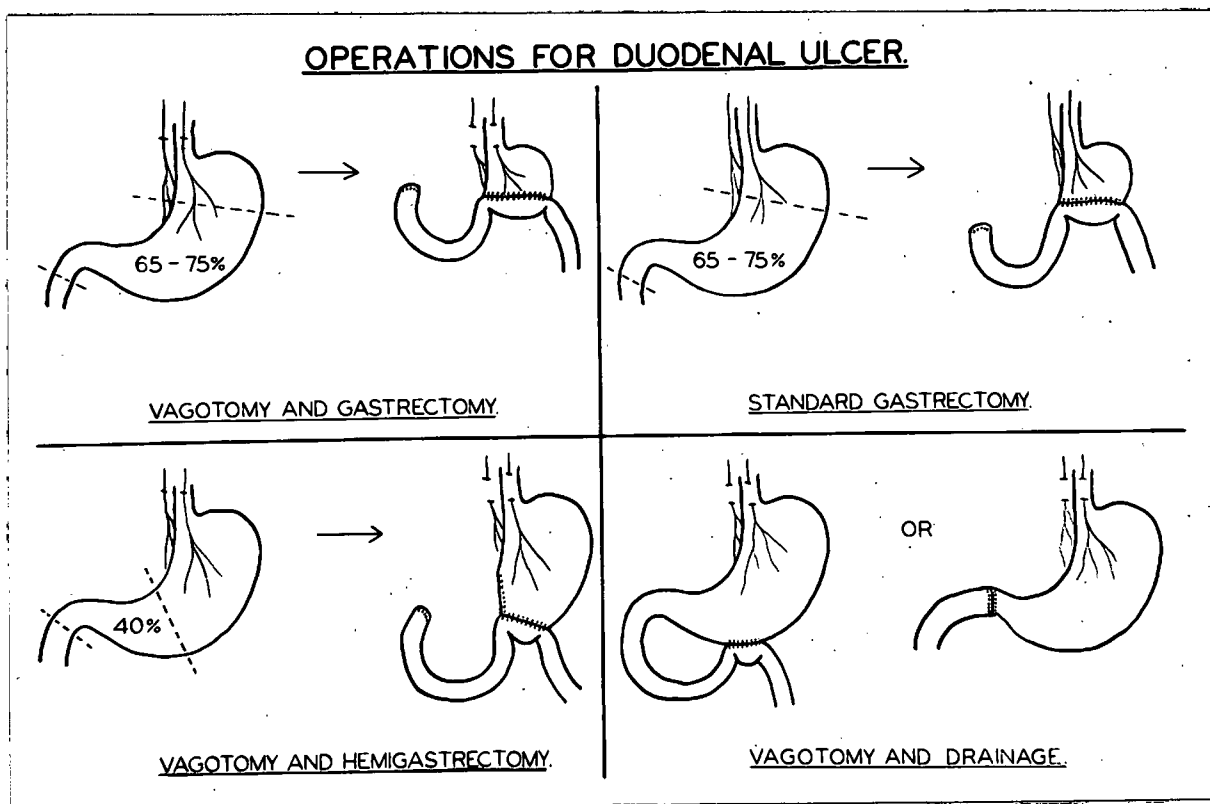


FIG. V.

Current Surgical Procedures in Duodenal Ulceration.

CHAPTER III.

INDICATIONS FOR SURGERY.

To-day the basic principles of surgical intervention in the treatment of duodenal ulceration are stabilised and fairly uniformly accepted, except for minor variations practised by different schools. This has not always been the case. Gastroduodenal haemorrhage was treated medically during the early part of the century with a prodigious mortality rate, until surgical intervention showed far better results. (Finsterer 1923).

x The indications for surgery remained haphazard until 1946
when Gordon-Taylor recommended "Selective surgical intervention".
(Gordon-Taylor 1946). It was Tanner in 1951 who laid down
the indications for surgery in peptic ulceration (Tanner 1951)
and thus firmly established the principles on which we are
still operating to-day.

In brief, the indications can be outlined as follows,
remembering that each case should be assessed on its own merits.

1. Failure of medical treatment or intractability in certain cases depending mainly on the age of the patient, psychological make-up, length of history and socio-economic considerations. 0

42/ 2. Complications:

2. Complications: (a) Haemorrhage.

Depending on the severity of this complication, emergency or elective procedures will be considered. Other considerations in this complication will be, the age of the patient, previous ulcer history, the presence of pain and other associated complications of duodenal ulceration.

(b) Pyloric obstruction due to scar stenosis.

(c) Perforation: (i) Acute. The majority will be treated surgically by simple closure of the perforation.

Depending on the time that has elapsed since the perforation occurred, conservative treatment may be considered. When perforation is associated with another complication such as haemorrhage, gastric resection may be indicated. Variations in method of treatment are practised in different centres.

(ii) Chronic
perforation or penetration.

3. The association of a gastric ulcer and duodenal ulcer.

4. Recurrence of ulceration.

CHAPTER IV.

SELECTION FOR SURGERY.

The final measure of success in duodenal ulcer surgery is the well-being of the patient. To achieve this the aim of surgery should be:

- (i) The cure of the presenting disorder, with minimal interference of normal function.
- (ii) The prevention of recurrent ulceration. To achieve this adequate reduction of acid secretion is essential.
- (iii) Low mortality.
- (iv) Low morbidity.

Throughout the years many workers have felt that removal of the major portion of the stomach for a benign condition like duodenal ulcer is a very drastic manoeuvre. That this is quite rightly so is evident from the numerous reports in the literature quoting figures of morbidity, mortality and post-surgery sequelae for the various procedures. Therefore, it is not surprising that improved knowledge of gastric physiology and its application to the surgery of duodenal ulcer has initiated the present era of physiological surgery. Previously the surgical treatment of duodenal ulcer was not planned on the basis of physiological investigation but on empirical trial

and clinical experience.

With the advent of the augmented histamine test as a reliable index of gastric acid secretion a large volume of data has accumulated on the secretory patterns occurring in patients suffering from duodenal ulceration (Gillespie, Kay 1961, Gelb et al 1961, Marks et al 1963, Orr 1962). That all duodenal ulcer patients are not hypersecretors and that a wide variation of secretory patterns exists, is quite obvious from these figures. A study of these patterns has suggested that the factors playing the dominant role in gastric acid secretion are not the same for all patients. A high basal secretion (BAO) does not automatically indicate vagal stimulation, but may be due to the hormonal element (Gillespie, Kay 1961) although this will only occur in the minority of cases. It seems rational then to add a vagotomy to any surgical procedure where a raised BAO is present.

The level of the maximal acid secretion (MAO) will serve as an index of the parietal cell mass (PCM) and if this is excessive, partial resection (antrectomy or subtotal) will have to be performed.

Those patients falling in between these groups can be submitted to a procedure which will reduce the acid secretion adequately in relation to the PCM. It must be realised that the

gastric acid secretion per se is not an indication for surgery, but only supplies valuable supportive data, allowing the surgeon to tailor the operation to the patient's individual needs.

The basis of sound medical practice remains accurate clinical evaluation of the patient as a whole and this applies no less to surgery. A complete assessment taking special note of age, sex, occupation, associated or previous disease especially tuberculosis, is as important as the degree of gastric acid secretion.

A rational policy of surgical selection can be formulated by keeping these considerations in mind and using the gastric acid secretion as estimated by the augmented histamine test.

The experience of various workers over the last 10 years has provided a large amount of data on the gastric acid secretions both in controls and in duodenal ulcer subjects and also in those patients with jejunal ulceration following gastrectomy and gastroenterostomy (Tables V and VI).

Selective surgery in duodenal ulceration has been advocated for a considerable time by various workers (Bruce et al 1959; Orr, 1962, 1963). Judging from the analysis of the results, it becomes obvious that selection gives considerably better results than a stereotyped procedure for all cases. Experience

has shown that certain rules are imperative in selection (Orr 1963).

- (i) If a raised basal secretion is present a vagotomy should be added.
- (ii) If a grossly excessive MAO is present a $\frac{3}{4}$ resection of FCM must be done.
- (iii) Where a duodenal ulcer is associated with a gastric ulcer the main attack should be against the duodenal ulcer.
- (iv) If the duodenum is short, fixed and scarred, a Billroth I anastomosis should be avoided because of the danger of leakage from the anastomotic line or skimping of the resection which will lead to recurrent ulceration.
- (v) Where a hemigastrectomy plus vagotomy is the procedure of choice with a fairly healthy duodenum a Billroth I anastomosis may be employed.

TABLE V.

SECRETORY MEANS OF B.A.O. AND M.A.O. IN CONTROLS, DUODENAL
ULCER AND JEJUNAL ULCER.

	MEAN B.A.O. mEq/hr.		MEAN M.A.O. mEq/hr.		REFERENCES
	M	F	M	F	
Controls	2.7 (31)	1.9 (15)	23.2 (31)	15.0 (15)	Marks, Shay, 1959 ^{and}
	2.5 (14)	1.3 (18)	22.4 (14)	14.6 (18)	Bruce et al 1959
	4.2 (35)	1.8 (26)	22.6 (35)	15.2 (26)	Marks et al 1963
Duodenal Ulcer	6.0 (176)	3.2 (61)	37.5 (176)	24.3 (61)	Bruce et al 1959
	6.8 (152)		37.0 (152)		Kay cited by Sircus 1959
	7.3 (484)	4.3 (120)	35.2 (484)	24.3 (120)	Marks, Bank 1963 personal comm.
Jejunal ulcer: Following Gastrec- tomy.	7.9 (10)	5.5 (4)	25.1 (10)	16.4 (4)	Marks et al 1963
	7.7 (14)		31.1 (14)		Bruce et al 1959
Following gastro- enterostomy	9.1 (4)		36.1 (4)		Marks et al 1963
	8.7 (10)		43.5 (10)		Bruce et al 1959

Number of patients in parenthesis

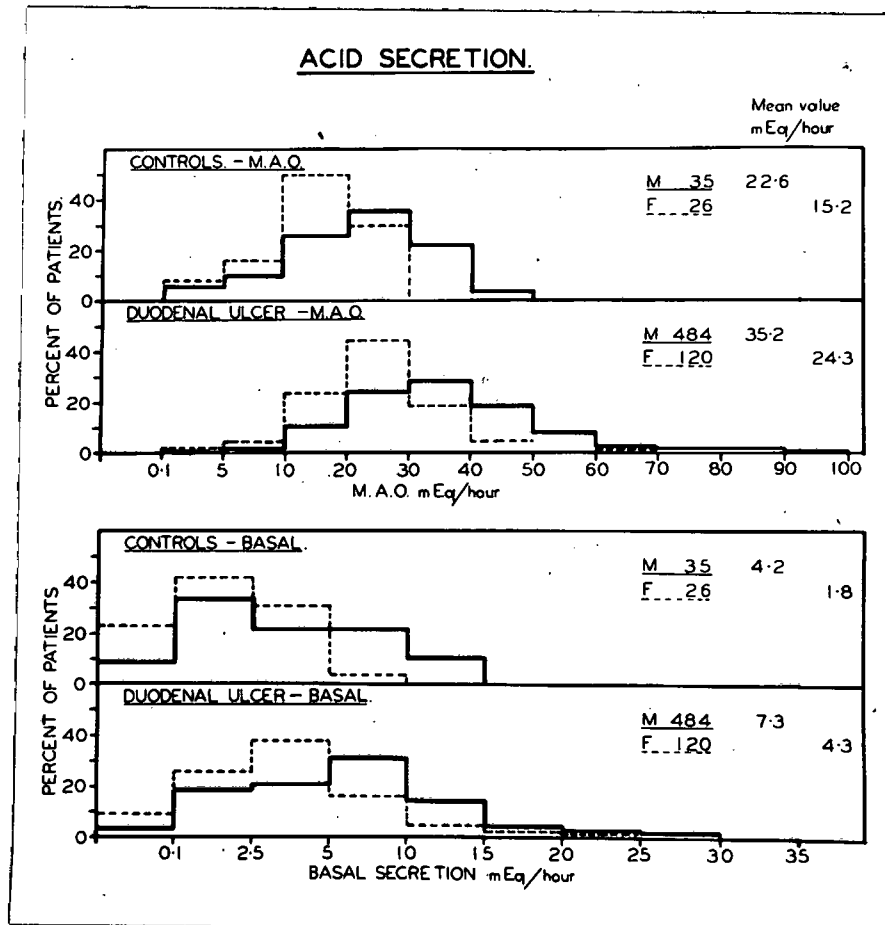


TABLE VI.

Histograms of BAO and MAO in controls and Duodenal Ulcer patients (Marks and Bank).

CHAPTER V.

AIM. AND POLICY OF SELECTION.

With the above criteria as a basis, a program of selective surgery for duodenal ulceration was started at Groote Schuur Hospital, the teaching unit of the Medical Faculty of the University of Cape Town, in January 1960, under the auspices of the departments of surgery and gastroenterology.

Utilising the experience of other workers (Johnson and Orr 1954) ⁶ (Bruce et al 1959) a policy of selective surgery was instituted. Accepting the BAO as an index of vagal activity and the MAO as representing the PCM, selection was advised according to Fig. VI.

- (i) Vagotomy was advised where (a) a drainage procedure was indicated ($MAO < 35 \text{ mEq/hr.}$) and (b) where an excessive basal secretion was present ($> 10 \text{ mEq/hr.}$).
- (ii) A certain amount of latitude was allowed for the patients with a BAO of less than 10 mEq/hr. with a MAO between $25-50 \text{ mEq/hr.}$ where either a hemigastrectomy plus vagotomy or a standard gastrectomy could be performed depending on the individual surgeon's preference.

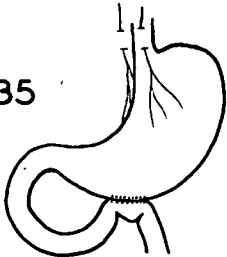
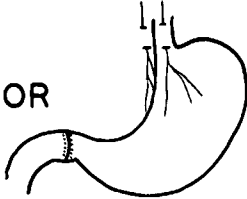
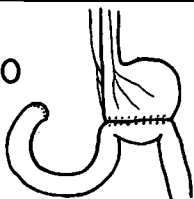
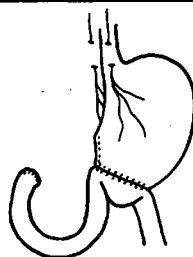
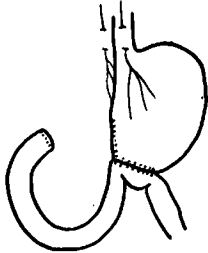
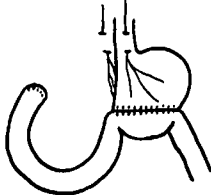
SELECTIVE SURGERY IN DUODENAL ULCER		
BASAL.	M.A.O.	OPERATION.
< 10	< 35	 OR 
< 10	25 - 50	 OR 
> 10	25 - 50	
> 10	> 50	

FIG. 6.

Selection of Procedure according to acid secretion in this series.

- (iii) In cases with an excessive BAO but with a moderate MAO a vagotomy was essential but a hemigastrectomy (antrectomy) was considered adequate.
- (iv) Where both excessive BAO and MAO were excessive a vagotomy plus standard gastrectomy was indicated.

Having followed this policy now for $3\frac{1}{2}$ years, two comparative series of cases have been established.

1. A selected group where the procedure of choice was performed according to the gastric acid secretion.
2. An unselected group where different procedures were performed for various reasons - e.g. (a) technical difficulties, (b) gastric acid secretion unknown, (c) surgeon's preference and experience, (d) physical condition of the patient, (e) association of a gastric ulcer with duodenal ulceration.

All emergencies were excluded from these two groups.

Such a programme would fail in its aim if it neglected to achieve reduction in gastric acid secretion to levels at which recurrent ulceration becomes unlikely. Likewise, it would fail if post-operative sequelae and mortality were not less than those previously obtained by a standard manoeuvre

like the 2/3 Polya gastrectomy which was performed for the majority of duodenal ulcer cases in the past.

The aim of this treatise is:

1. To determine the extent of acid reduction obtained in individual procedures.
2. To ascertain the prognostic value of such reduction.
3. To give an evaluation of the results of this policy of selective gastric surgery in the treatment of duodenal ulcer.
4. To make pertinent recommendations regarding future policy if and where indicated.

P A R T I I .

Chapter I.

METHOD OF STUDY.

A. MATERIAL. (Table VII)

During the $3\frac{1}{2}$ year period under review a total of 1160 cases of duodenal ulceration attended Groote Schuur Hospital. Of these 421 were submitted to surgery; 380 had elective gastric surgery and the remaining 41 had emergency operations. Two hundred and forty seven (65%) of the 380 patients subjected to elective surgery and 17 (41.5%) of the 41 patients who had emergency procedures were followed up in detail. The incidence of the sexes in the different racial groups are also reflected in this figure.

Acute Perforations. One hundred and four cases of acute perforation were seen during the $3\frac{1}{2}$ year period. Of these 91 had surgical intervention and 55 were subsequently followed up.

Re-operations. Sixteen corrective procedures were performed for post-operative sequelae in patients where the primary intervention was performed within this $3\frac{1}{2}$ year period.

B. ACID STUDIES. (Table VIII)

Six hundred and four of the total number of 1160 cases were submitted to acid secretory studies by the augmented histamine test. Two hundred and seventy eight of the 380 patients who had elective surgery had pre-operative acid studies and in 130 of these, the test was performed post-operatively. In the patients who had
.... emergency

MATERIAL.

JAN. 1960 - JUNE 1963.

NUMBER OF DUODENAL ULCERS. . . . 1160

NUMBER SUBMITTED TO SURGERY. . . . 421

E - EUROPEAN

C - COLOURED

B - BANTU

M - MALE

F - FEMALE

	SURGERY.						FOLLOWED UP.					
ELECTIVE	380						247 (65%)					
	E		C		B		E		C		B	
	207		164		9		144		96		7	
	M	F	M	F	M	F	M	F	M	F	M	F
	156	51	134	30	8	1	107	37	76	20	7	-
EMERGENCY	41						17 (41.5%)					
	E		C		B		E		C		B	
	27		13		1		9		7		1	
	M	F	M	F	M	F	M	F	M	F	M	F
	22	5	8	5	1	-	8	1	4	3	1	-
TOTAL	421						264 (62.7%)					
	E		C		B		E		C		B	
	234		177		10		153		103		8	
	M	F	M	F	M	F	M	F	M	F	M	F
	178	56	142	35	9	1	115	38	80	23	8	-

TABLE VII.

Material January 1960 - June 1963 showing: number, racial and sex incidence of patients in elective and emergency groups who were submitted to surgery, and number followed up in each group.

TABLE VIII.

ACID STUDIES.

Jan. 1960 - June 1963.

Total number acid studies performed:			604
Acid studies in cases submitted to surgery:			
	Pre-op.		Post-op.
Elective	278		130
Emergency	<u>3</u>		<u>10</u>
Total:	281		140

emergency surgery only 3 had pre-operative and 10 postoperative acid studies.

Acute Perforations. Sixty-eight of the 104 patients in this group had acid studies following perforation.

C. TECHNICAL METHODS.

1. Augmented histamine test.
2. Insulin test.

THE AUGMENTED HISTAMINE TEST.

While the augmented histamine test is simple and may be carried out by an experienced technician, the majority of the tests in this series were done personally and the remainder under strict supervision. Constant supervision is necessary while the test is in progress, as energetic and conscientious emptying of the stomach is essential, as well as strict observance of the physical condition of the patient.

This test was popularised by Kay (Kay 1953) and Marks (Marks 1961).
Technique. An 8 - 9 hour fast precedes the test, (usually from midnight the previous night) and it is performed the next morning at about 8 - 9 a.m. The duration of the test roughly requires two hours to complete.

58/Equipment.

Equipment. (Fig. VII and VIII)

1. Radio-opaque Levin nasogastric tubes (Rüsch) - sizes 14 - 16
2. $\frac{1}{2}$ " rubber tubing and glass connections.
3. One 250 ml. collection tube with doubly perforated rubber stopper.
4. Overflow flask.
5. Weak suction pump - 5 mm. Hg.
6. Six large test tubes - size $1\frac{1}{2}$ " x 8" - volume 200 ml.
7. Couch with adjustable head section.
8. Syringes: (a) 50 ml. with wide connection for aspirating nasogastric tube.
(b) Two 5 ml. syringes with hypodermic needles of assorted sizes.
9. Drugs: (a) Antihistaminic (mepyramine maleate - neoantergan, anthisan) - 50 mgs. ampoule.
(b) Histmine acid phosphate - 10 ml. ampoule with 1 mg. per ml.
(c) Liquid paraffin.
10. Disposable cardboard mug, paper tissues, $\frac{1}{2}$ " wide adhesive tape.
11. X-Ray machine with an attached fluorescent screen.

Insertion of Levin Tube.

The procedure is carefully explained to the patient. The patient is seated in a chair and handed a mug and a few tissues. The nasogastric tube is selected according to the size of the



FIG. VII.

Radio-opaque Levin tubes.
Assorted syringes and needles.
Antihistaminic.
Histamine acid phosphate.
Cotton wool swabs.
Commercial ether.

patient. It is better to pass a bigger size in stout and obese patients for it is more easily visualised on screening. The selected tube is then lubricated with liquid paraffin and passed through the nose. Inserting it via the latter route is essential for its maintenance in the desired position. It is difficult to maintain the tube in its correctly placed position if passed orally because of the continual action of the buccal muscles and tongue in getting rid of accumulated saliva. The tube is passed through the nostril in a slightly downward direction with the head slightly extended to straighten out the curvature of the naso- and hypo-pharynx. The patient is instructed to breathe deeply and to swallow all through the procedure. Coughing and stridor means the tube has gone into the trachea and it should then be withdrawn a few inches and re-inserted. A moderate amount of gagging may be experienced, caused by the irritation of the pharynx.

Once the tube passes into the oesophagus a slight tug will be felt with each swallow and it will slip down quite smoothly.

The proximal end of the Levin tube is marked by concentric black rings - in the usual type these are 4 inches apart but some tubes may be marked at 8" intervals. When the tube is inserted past the first ring a knot is tied in the tube and screening is proceeded with.

Screening. The patient stands behind the screen facing the examiner. Females should not wear any tight corsets or foundation garments.

The position of the tube is then visualised under the screen.

The correct position for the tip of the tube should be on the left side of the vertebral column and adjacent to it. It usually lies in a gentle curve from the cardia through the body of the stomach. This position is just proximal to the antrum of the stomach both in the erect and supine positions. In most vertical-lying stomachs this position is virtually in the pelvis. In transverse lying stomachs it is much higher. Once the tube is in the correct position it is maintained there by strapping it down securely with adhesive tape to the side of the face.

Occasionally the tube will be coiled up in the fundus of the stomach. It should then be withdrawn as far as the cardia and gently re-inserted again, whilst visualising its progress under the screen, requesting the patient to breathe deeply in and out. Invariably it will slide down into the desired position. If difficulties are encountered tight undergarments may be the cause and should be removed.

The same procedure is followed in post-surgery patients. In these the tube will usually go straight into the correct position. The difficulty in these patients is, that if it is inserted too far, it will go straight through the stoma into the small bowel. It is therefore essential to know beforehand what type of operation was performed on the particular patient.

If the patient has had a gastroenterostomy the tube can be inserted fairly far down into the stomach but not quite as deep as

in the pre-operative case. On the other hand if the patient had a gastrectomy then the tip should only be visualised 2 - 3 inches below the dome of the left leaf of the diaphragm.

Once the tube is securely fixed the patient is put on a couch, the head section raised so that he reclines comfortably with his head and shoulders moderately elevated. He is advised not to swallow any saliva after the tube is positioned but to spit it out into the supplied cardboard mug.

Suction. (Fig. VIII)

The Levin tube is connected to the 250 ml. collecting tube; this is connected in series to the overflow flask, which in turn is connected to the suction pump. Suction is maintained at approximately 5 mm. Hg.

The rubber stoppers of these collecting flasks should be securely applied so that no leak in the circuit can occur.

Following this, the collection of gastric juices is started and six selections are made:

1. Fasting collection.
2. 2 x 30 minute basal collections.
3. 3 post histamine collections.
 - (a) 15 minutes.
 - (b) 30 minutes.
 - (c) 15 minutes.

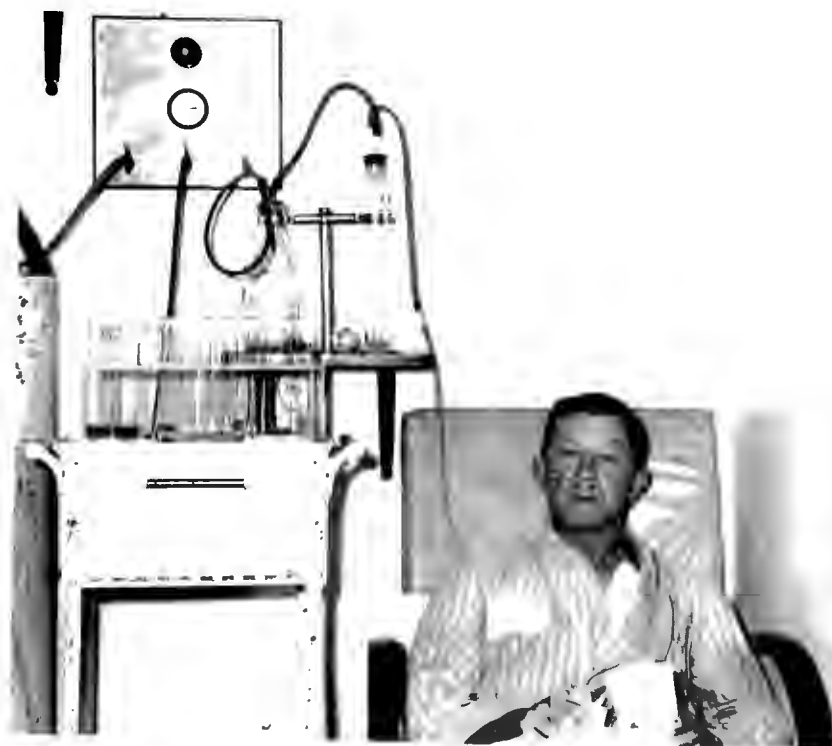


FIG. VIII.

Augmented Histamine Test in progress.

1. Fasting.

This first collection will contain swallowed saliva, mucous and sometimes bile due to reflux and occasionally a small, negligible quantity of blood. Continuous suction should be applied and manual aspiration done every 5 minutes. Fifty ml. of air is introduced with a syringe and all gastric juice manually aspirated. The insertion of air also blows the tip of the tube off the gastric wall in case it has been sucked onto the wall. No violent force should be used but with gentle suction the stomach can be kept empty efficiently. This collection must be persisted with until no more mucous, saliva or bile-stained juice is obtained. This specimen is labelled the fasting juice. If persistent bile-stained juice is obtained the tube may be slightly withdrawn. If any difficulties are experienced, re-screening the patient and readjustment of the tube may be necessary. The juice collected over this period is emptied into the first of the 6 large test tubes (200 ml.) provided for the test. This aspect of the procedure usually takes 5 - 15 minutes. The volume of juice varies tremendously from patient to patient but is usually higher in patients with duodenal ulceration. It may be anything from 0 to 200 ml.

2. Basal Secretion.

The gastric contents are aspirated for the next hour. Every 5 minutes the stomach must be manually emptied and the patency of the tube established. After half an hour the juice is decanted

65/ into

into test tube number 2 and this is labelled B.1 (Basal 1).

At this stage 50 mgs. (2 ml.) anthisan is given intramuscularly. This counteracts most of the side effects of the histamine to be given at a later stage of the test. Another half hour collection is made, poured into test tube number 3, and labelled B.2 (Basal 2).

3. Histamine.

At the end of an hour, histamine acid phosphate 0.04 mg./kg. body weight is injected subcutaneously. The patient should be warned that this will have a transient flushing effect and that the injection will be slightly painful and burning. These two latter effects can be minimised by using a very fine hypodermic needle and giving the histamine very slowly. If the calculated dosage of histamine comes to less than 2 ml. a minimum of 2 ml. must be administered. We usually add about 0.2 ml. to the calculated dosage.

The next 3 collections are then made very accurately over the next hour, i.e.

15 minutes, labelled H.1 (Histamine 1)

30 minutes, labelled H.2 (Histamine 2)

15 minutes, labelled H.3 (Histamine 3) respectively.

The side effects of histamine used in this way are very few.

Occasionally the patient may feel slightly dizzy, sweaty and very rarely a moderate shock-like state may be encountered. This is

quite easily corrected by lying the patient flat with elevation of the feet. It is very rarely necessary to abandon the test because of side reactions.

Titration.

We measure:

1. Basal acid output (BAO) in milli-equivalents hydrochloric acid per hour (mEq/hr).
2. Maximal acid output (MAO) in milli-equivalents hydrochloric acid per hour (mEq/hr).
3. Maximal histamine response (MHR) equals mEq. hydrochloric acid in the mid half hour (H.2) collection.

The final results are obtained by titrating the collected specimens against N/10 sodium hydroxide using Töpfers reagent for "free acid" and phenolphthalein for "total acidity" as indicators.

Titration Procedure. (Fig. IX)

The volume of each collection is measured and noted. The constituents of each collection e.g. bile, mucous, blood are recorded.

Five ml. aliquots of each collection is measured into a small Ehrlenmeyer flask and a few drops of Töpfers reagent and phenolphthalein are added to each.

The 1/10 N. NaOH is prepared by using 1 ampoule of Titrisol (Taeuber and Corrsen) and adding sterile water to 1 litre. This preparation should not be left open as the concentration may change due to absorbed carbon dioxide.

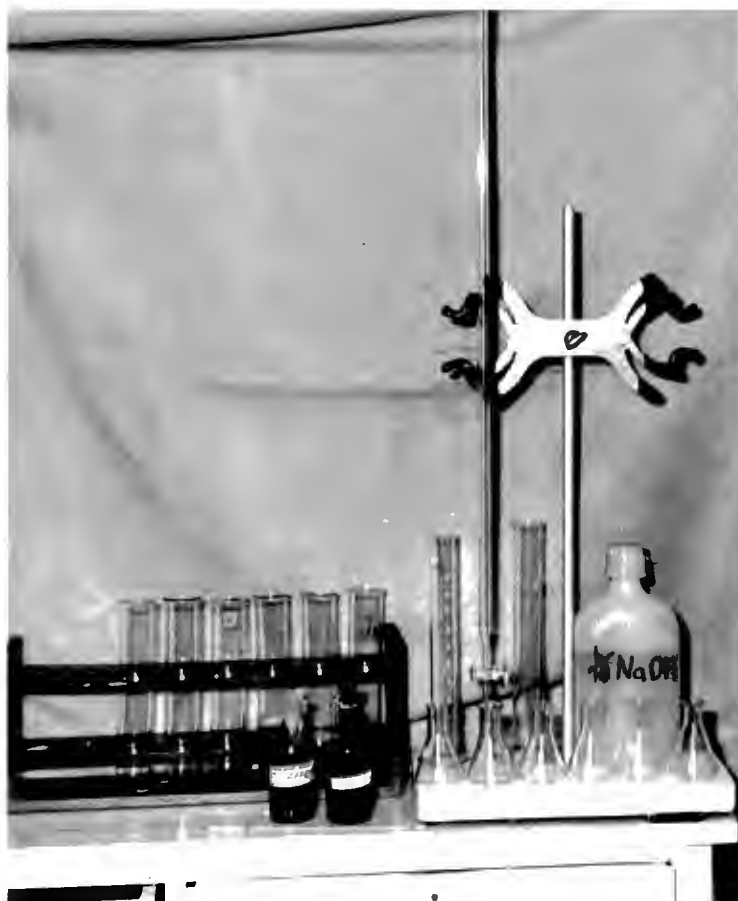


FIG. IX.

Titration Equipment.

A graduated 50 ml. burette is placed in a burette stand and only filled with 1/10 N. NaOH immediately prior to starting the titration.

If free acid is present in the sample to be tested ($\text{pH} < 3.5$) a red colour will appear with the addition of Töpfer's reagent and the pH may then be anywhere between 0 and 3.5. Before titration is started the burette reading is noted. Start titrating the sample with 1/10 N. NaOH. A change from red to yellow will occur at pH 3.5, the change point of Töpfer's. At this point the burette reading is noted again. Calculation of this value will denote "free acid". Titration is then continued until the specimen turns from yellow to salmon pink taking this to be at a pH of approximately 7 the change point of phenolphthalein and calculation of the total amount of 1/10 N. NaOH used will denote "total acid". This is repeated with each of the 6 specimens collected.

In Cape Town the figures we use for BAO and MAO are the "total acid" values calculated.

If a considerable quantity of blood is present in the specimen to be titrated, the exact points of colour changes may be very difficult to assess accurately. In these circumstances the specimen can be left overnight; the erythrocytes will form a sediment at the bottom of the specimen and a relatively clear supernatant fluid for titration can be pipetted off the next morning. Gastric juice does not lose or change its acid content by being kept for any period of time.

Calculation. (Fig. X)

Total acid:

1. Concentration in mEq/litre i.e.
ml. $1/10$ N. NaOH $\times 20$ = mEq/litre
2. Output in mEq/hour = concentration (1) \times volume
of whole specimen divided by 1000.

BAO is equal to sum of the values obtained for the two basal half hours.

MAO is equal to the sum of the values obtained for the three posthistamine specimens.

MHR is equal to the value obtained for the middle posthistamine half hour. This parameter is not used in Cape Town.

If the pH is more than 3.5 (no red colour obtained with addition of Töpfers reagent) it means that no free acid is present in the specimen. The pH of the specimen is then measured electrometrically. If the pH is below 6 the MAO is arbitrarily taken as 0.1 mEq/hr. If the pH fails to drop below 6 as measured on the pH meter (Fig. XI) titration is valueless and the MAO = 0 and the BAO in the latter two instances will automatically be nil.

Performing the augmented histamine test in patients after gastrectomy or a drainage procedure is more difficult. In these, one usually finds a large amount of bile and pancreatic juice reflux contaminating the specimen. Readjustment of the tube in these cases without re-screening may result in the complete retraction from the stomach. Initial placing of the tube is more difficult

GROOTE SCHUIJER HOSPITAL.

GASTRO-INTESTINAL SERVICE - J.I.

AUGMENTED HISTAMINE TEST.

NAME: NUMBER:

AGE: WEIGHT: HEIGHT:

WARD: DATE: DIAGNOSIS:

Spec.	Time	Vol.	Bile RBC's	Acidity.		Acid Output		PH
				Fa.	mEq./L Ta.	Fa.	mEq.	
Fasting								
Basal 1.								
Basal 2.								
Post Hist. 1								
2								
3								
4								

MHR. MAO.

COMMENT:

SUGGESTIONS:

FIG. X.

Gastric Acid Calculation Form.

Fa = free acid.

Ta = total acid.



FIG. XI.
pH - Meter.

because of previous surgery and re-screening may be necessary. With experience one soon is able to judge the amount of manipulation necessary to achieve the best results.

The augmented histamine test in this series has been performed in exactly the same manner in the post-operative as in the pre-operative patients. Previous workers have used a special stomal blocking balloon (Marks, 1951). Stevens and Kyle (Stevens, Kyle, 1963), comparing stomal blocking and non-stomal blocking methods have shown that there is no significant difference in the values of gastric acid obtained by using these two methods.

If the stomal blocking method is employed one does not get a true perspective of the physiological state of the gastric contents e.g. volume and degree of bile and pancreatic juice reflux.

INSULIN TEST.

In a certain proportion of cases this test was performed for the completeness of vagotomy.

Technique.

The patient is prepared in the same way as for the augmented histamine test. The Levin tube is positioned in a similar way as for all post-surgery cases, depending on the previous operation, and observing the same strict criteria as for the histamine test.

Electrical and manual suction is applied long enough to aspirate all fasting juice and swallowed saliva. The basal secretion is then collected over the next hour, dividing this collection into two

half hour periods. At the end of this hour 15-20 units of crystalline insulin is injected intravenously and the gastric juice collected for the next two hours, dividing the collections into four half-hour specimens.

Calculation.

If titratable acid is present the total acid for each individual specimen is calculated as for the augmented histamine test by titrating with 1/10 N. NaOH using Töpfer's reagent and phenolphthalein as indicators. If free acid is absent the pH of each collection is determined electrometrically.

Interpretation.

This is indeed a very difficult problem and no uniformity of opinion for completeness of vagotomy is held. Each worker using this test has his own criteria for completeness. Bachrach (Bachrach, (1963) reviewing the value of this test, considers all aspects from the time Hollander (Hollander, 1948) described the test. He critically examines the interpretations of subsequent workers (Roth, Bockus, 1951), (Stempien et al 1958), (Waddell, 1957). Considering also other methods e.g. motility as an index of completeness (Stein^{and}, Meyer, 1948), the stimulation of gastric secretion by intravenous alcohol (Hirschowitz et al, 1956), he came to the conclusion that this test is not ideal because no fixed numerical values are defined but that it is at present the most satisfactory procedure available. This writer recommends certain suggestions for the clinician:

- (i) Two hour basal and three hour post-insulin estimations.
- (ii) If the post-insulin acid output in any hour does not exceed the higher of the 2 basal hours, a complete vagotomy can be assumed.
- (iii) If no free acid is secreted, the ability of the stomach to secrete acid must be tested by the augmented histamine test. If no acid is secreted, the augmented histamine test should be repeated and if again negative, the patient is achlorhydric whether from vagotomy or some other reason. If, however, acid is secreted it should immediately be followed by a Hollander test.
- (iv) If the post-insulin secretion exceeds the basal it suggests that some parasympathetic supply to the stomach is present. If, however, the increase is so little as to appear to be within the range of spontaneous fluctuations e.g. 1 mEq or less; such increase should be ignored and completeness of vagotomy assumed. The higher the post-insulin acid rise, the greater the possibility that the vagi are intact.
- (v) A basal reaching 2 mEq/hour suggests an incomplete vagotomy and if the post-insulin secretion does not show a clear increase above the basal output, the test should be repeated.

Because of the difficulties of interpretation it has been suggested by Hunt (Hunt, (1956) that maximal histamine stimulation

may supplant insulin stimulation for evaluation of the post-operative gastric secretory state with or without vagotomy. Gelb et al (Gelb et al, 1961) support the thesis that complete vagotomy markedly reduces the secretory response to histamine.

Performing the Hollander test as already described, a vagotomy is considered incomplete if:

- i. There is a significant increase in volume of gastric juice secreted in the post-insulin period as compared with the basal volume.
- ii. ^{There is} A drop of 1 pH unit as measured electrometrically in specimens where no free acid is present.
- iii. Free acid is present and acid titrations performed show a rise of more than 1 mEq/hr over the basal estimation.

Applying these criteria there is still a group of patients where interpretation is extremely difficult, the main difficulty being bile reflux. In this group vagotomy was reported as adequate if the acid secretion was such that jejunal ulceration was unlikely.

D. FOLLOW-UP.

A detailed analysis was made of every individual case report of those cases who had an operation for duodenal ulceration and entered on a special gastrointestinal work chart (Fig. XII). All cases were circularised with a letter requesting them to attend the department of gastroenterology, explaining the reason for such a request. A questionnaire (Fig. XIII) was included for completion by those unable to attend.

PEPTIC ULCER WORK CHART.				
NAME:.....		NO:		
ADDRESS:.....		PHONE:		
AGE:.....SEX:.....RACE:.....OCCUPATION:.....				
<u>HISTORY:</u> Duration:		Family History:		
Presenting Symptoms:				
<u>EXAMINATION:</u> <u>General:</u>		<u>Local:</u>		
<u>Associated Disease:</u>		<u>Side Room:</u>	<u>Blood group:</u>	
		Occ.Bl.		
		E.S.R.		
		Hb.:		
<u>MEDICAL TREATMENT:</u>		<u>Duration:</u>	<u>Drugs:</u>	<u>Hospital:</u> <u>Admissions:</u>
<u>COMPLICATIONS:</u>		<u>Perforation:</u>	<u>Bleeding:</u>	<u>Stenosis:</u>
<u>S.I.:</u> <u>Ba Meal.</u>	<u>A.M.TS.</u>	<u>DAO</u>	<u>Cytology:</u>	<u>Gastroscopy:</u>
MAO				
<u>SURGERY:</u>				<u>DATE:</u>
<u>HISTOLOGY:</u>				
.....				
.....				
.....				
<u>POST-OP:</u>	COMPLICATIONS		IMMEDIATE	
			SYMPTOMS:	

FIG. XII.

Copy of Peptic Ulcer work chart for
Pre-operative Data.

- FIG. XIII.

Copy of Questionnaire.

- 2 -

POST-SURGERY COMPLICATIONS :

Period:

Symptoms:

Examination:

<u>INVEST.</u>	<u>IHT.</u>	<u>BAO</u>	<u>Ba Meal</u>	<u>Gastroscopy</u>
		<u>M/O</u>		

<u>Hb:</u>	<u>Pancreatic Functions.</u>
<u>Serum Calcium.</u>	<u>Xylose.</u>
<u>Serum Iron.</u>	<u>Radioactive Fat.</u>
<u>Glucose Tolerance.</u>	<u>Jejunal Biopsy.</u>

TREATMENT: Medical.

Surgery.

RESULTS:

DEATH: CAUSE:

FIG. XIV.

Copy of Peptic Ulcer Work Chart for Post-operative Data.

Of those who were personally interviewed a detailed documented analysis of their post-operative state was made and entered on a special gastrointestinal work chart (Fig. XIV). All post-surgery sequelae encountered were investigated and treated. Where practical the augmented histamine test was performed and in a certain number the insulin test for the completeness of vagotomy was performed.

Evaluation of Results.

x This was established according to mortality, recurrent ulceration and the clinical grading as devised by Visick (Visick, 1948) and his colleagues (Pulvertaft, 1952) (Table IX) excluding recurrent ulcers from Grade V which are quoted separately.

A further critical analysis was made of the incidence of individual post-surgery symptoms for each procedure. These were recorded as positive even if elicited on direct questioning.

Difficulties.

In a country the size of South Africa, dealing with different racial groups, such a follow-up is fraught with difficulties.

In a teaching hospital like Groote Schuur, drawing material from all the provinces and from even outside its boundaries, (sometimes from as far afield as 2,000 miles), it becomes an economic impossibility for many patients to attend in person.

Many of our coloured population frequently change their places of domicile for various reasons, without leaving forwarding addresses

TABLE IX

CLINICAL GRADING.

<u>GRADE.</u>	<u>SATISFACTORY.</u>
I.	No gastric symptoms.
II.	No pain; mild occasional symptoms easily controlled by care.
III.	Mild symptoms, not controlled by care but not interfering with enjoyment of life or work.
	<u>UNSATISFACTORY.</u>
IV.	Same as Grade III but symptoms do interfere with enjoyment of life or with work.
V.	Not improved; severe symptoms (excludes patients with recurrent ulcers).

making it impossible to trace them by any means. This applies even more to our Bantu patients coming from the reserves, constituting a migratory labour force.

Any study of this nature, therefore, must content itself with a much smaller percentage follow-up than places with much bigger and more stable populations, concentrated in a smaller area.

Chapter II.

RESULTS

RACIAL AND SEX INCIDENCE. (Table X)

Of the 421 cases (elective and emergency) submitted to surgery for duodenal ulceration, 42.3% were European males, 27.3% coloured males and 2.1% Bantu males, with European and coloured females contributing 14.4% and 8.3% respectively. Relative to outpatient attendances, the incidence of surgically treated duodenal ulceration was somewhat lower in the coloured as compared to European population (about 50%). The incidence of surgically treated duodenal ulceration in the Bantu is very much lower than in the European or coloured, viz. about 10% of the European incidence. This very low incidence of duodenal ulceration in the Bantu was even more striking in the case of Bantu females, in whom only one case was encountered - excluding 2 Bantu females in whom duodenal ulceration was associated with the Zollinger-Ellison syndrome. These 2 cases will be discussed in a later chapter. The sex distribution in the European and coloured population was similar. The

... ratio of

MATERIAL.
JAN. 1960 - JUNE 1963.

NUMBER OF DUODENAL ULCERS. . . . 1160
NUMBER SUBMITTED TO SURGERY . . . 421

E - EUROPEAN } M - MALE
C - COLOURED } F - FEMALE
B - BANTU

	SURGERY.	FOLLOWED UP.
ELECTIVE	<p style="text-align: center;">380</p> <pre> E C B 207 164 9 / \ / \ / \ M F M F M F 156 51 134 30 8 1 </pre>	<p style="text-align: center;">247 (65%)</p> <pre> E C B 144 96 7 / \ / \ / \ M F M F M F 107 37 76 20 7 - </pre>
EMERGENCY	<p style="text-align: center;">41</p> <pre> E C B 27 13 1 / \ / \ / \ M F M F M F 22 5 8 5 1 - </pre>	<p style="text-align: center;">17 (41.5%)</p> <pre> E C B 9 7 1 / \ / \ / \ M F M F M F 8 1 4 3 1 - </pre>
TOTAL	<p style="text-align: center;">421</p> <pre> E C B 234 177 10 / \ / \ / \ M F M F M F 178 56 142 35 9 1 </pre>	<p style="text-align: center;">264 (62.7%)</p> <pre> E C B 153 103 8 / \ / \ / \ M F M F M F 115 38 80 23 8 - </pre>

TABLE X.

ratio of males to females in European patients was 3.2:1 and in coloured patients 4.0:1.

COMPARATIVE RESULTS (Table XI).

One hundred and ninety four of the 380 elective cases were selected according to gastric acid secretion studies, as defined in Part I, Chapter V. The remaining 186 formed the unselected group.

The number of each individual procedure is shown in Table XI. It will be seen that Standard Polya Gastrectomy accounted for about half of the definitive procedures and hemi-gastrectomy and vagotomy for roughly a quarter. The vast majority of Standard Polya gastrectomies were carried out as unselected procedures whereas vagotomy combined with either pyloroplasty, gastro-enterostomy, standard gastrectomy or hemi-gastrectomy were performed chiefly as selected operations.

DEFINITIVE PROCEDURES.

No: 380

PROCEDURE	SELECTED	UNSELECTED	TOTAL
PYLOROPLASTY	1	—	1
PYLOROPLASTY + VAG.	22	2	24
GASTRO-ENT.	1	1	2
GASTRO-ENT + VAG.	38	15	53
STANDARD POLYA	41	131	172
STANDARD POLYA + VAG.	24	—	24
HEMI-GASTR + VAG.	67	37	104
TOTAL	194	186	380

TABLE XI.

CHAPTER III.

RESULTS OF INDIVIDUAL PROCEDURES.

I. STANDARD GASTRECTOMY.

This procedure was performed in 172 cases. Of the 380 elective cases under review, this procedure contributed by far the biggest group. All the 172 were of the antecolic Polya variety, except one case where a retrocolic anastomosis was performed. A Hofmeister valve was constructed in all except 2.

Of the 172 cases, 41 were selected and 131 unselected.

Follow Up (Table XIIa):

Twenty six of the selected group and 83 of the unselected cases were followed up - a total follow up of 63.4%.

Racial and Sex Incidence (Table XIIb):

Females constituted 15.7% of this group and 32.9% of all females subjected to surgery. This 15.7% is appreciably less than in the vagotomy plus drainage groups. Three of the total of 9 Bantu males present in this series were in this group.

Acids (Table XIIc):

Of the 41 patients comprising the selected group according to acid studies, 12 had post-operative acid

... studies

STANDARD GASTRECTOMY.

TABLE XIIa

	SELECTED	UNSELECTED
NUMBER: 172	41	131
FOLLOWED UP	26	83
TOTAL % FOLLOW UP	63.4	

TABLE XIIb

Racial & Sex Incidence

	EUROPEAN		COLOURED		BANTU	
	M	F	M	F	M	F
NUMBER: 172	84	15	58	12	3	-
FOLLOWED UP: 109	58	10	31	7	3	-

TABLE XIIc

Acids.

	NO.	SELECTED	NO.	UNSELECTED
		Mean and Range mEq/hr.		Mean and Range mEq/hr.
PRE-OP.	41	BAO 5.0(0.8-8.8) MAO 35.6(28.8-46.6)	53	5.7(0-17.0) 24.3(3.1-50.1)
POST-OP.	12	BAO 1.2(0.0-2.4) MAO 2.3(0.0-10.2)	40	0.8(0-7.3) 3.0(0-17.1)
% MEAN REDUCTION		BAO 74 MAO 93.5		BAO 86 MAO 87.6

studies; 53 of the 131 unselected group had pre-operative acid studies and 40 post-operatively. The outstanding difference, comparing the pre-operative values in these 2 groups, is that the MAO in the unselected group was appreciably less than in the selected group, (about 10 mEq./hr.). The reason for this difference is probably due to the fact that 67.9% of the 53 unselected cases who had pre-operative acid estimations could have had a vagotomy plus drainage procedure performed. In 26.4% of the unselected group, the pre-operative BAO was over 10 mEq/hr. and should have had a vagotomy as an added procedure according to our policy of selection. In one case, a standard gastrectomy and vagotomy was indicated but a hemi-gastrectomy was done and a jejunal ulcer had already developed (Case Report I).

Total achlorhydria was only encountered in 1 case (8.3%) post-operatively in the selected group, but in 6 (15%) of the unselected group (histograms - Figs. XV and XVI).

Gastric acid secretion was reduced about 80% and 90% for the BAO and MAO respectively with this procedure for both selected and unselected groups.

... Post-Operative

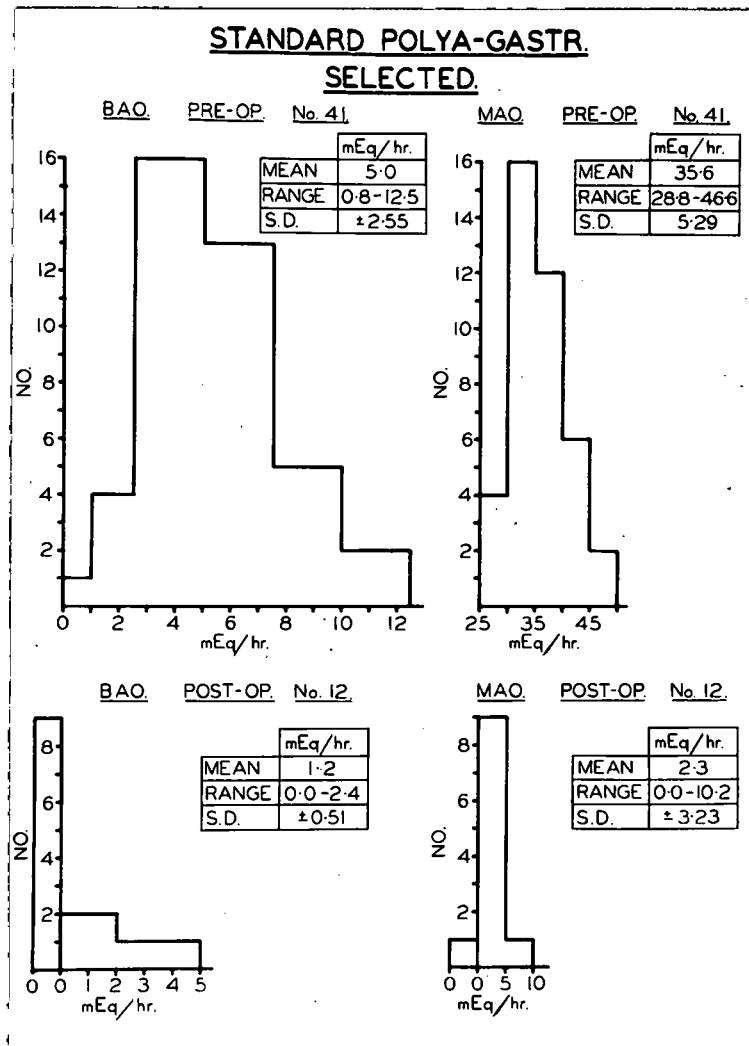


FIG. XV.

Histograms of pre- and post-operative BAO and MAO in selected group of standard Polya gastrectomy.

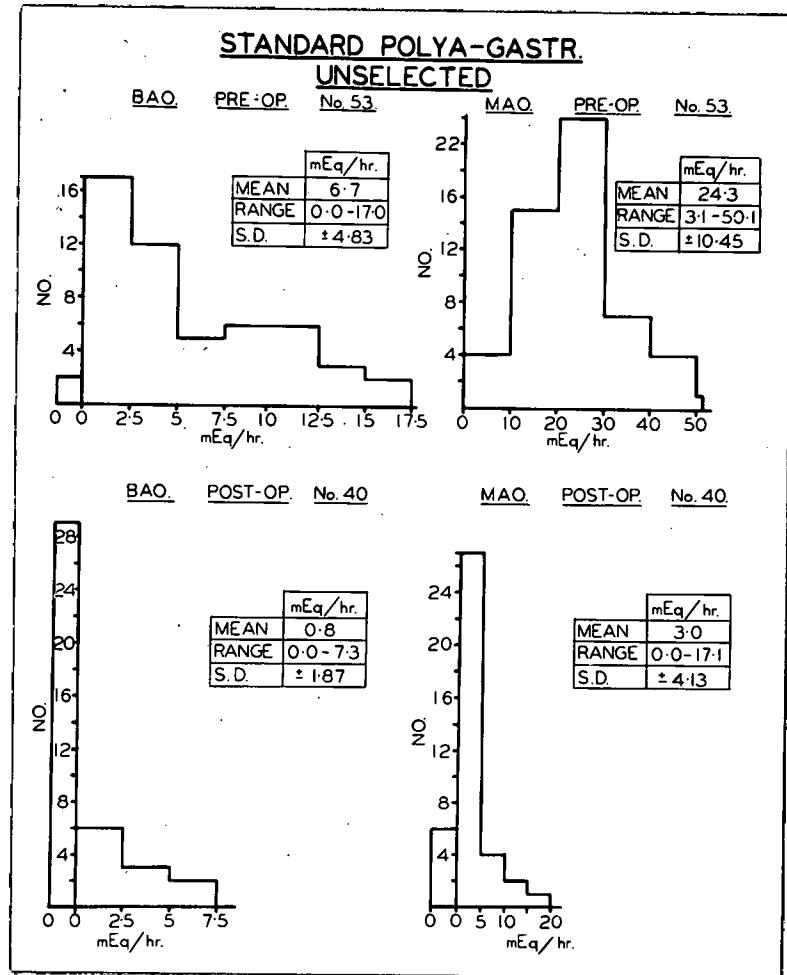


FIG. XVI

Histograms of pre- and post-operative BAO and MAO in unselected group of standard Polya gastrectomy.

Post-Operative Status (Table XIId):

One patient (1.2%) in the unselected group died post-operatively. This was the only fatality in the elective procedures in this series.

Recurrent ulceration occurred in 4 cases (4.8%), again in the unselected group.

Of the selected group, 96.1%, and of the unselected only 80.2% cases could be classified as satisfactory.

Serious Complications (Table XIIE):

A marked difference is observed between the selected and unselected groups when the incidence of serious complications is analysed. In the selected group only 1 patient (3.9%) suffered from severe dumping and vomiting. This case still requires intensive medical therapy. It was interesting to note that the gastrectomy in this instance was performed without a Hofmeister valve. Corrective surgery was not carried out during the period of follow up in this group.

Ten of the 16 patients comprising the 19.8% poor results in the unselected group already had corrective surgery for post-gastrectomy sequelae - 2 for afferent loop stasis, 4 for efferent loop obstruction and 4 for jejunal ulceration. The remaining 6 patients are on

... intensive

STANDARD GASTRECTOMY.

TABLE XIId

POST-OPERATIVE STATUS	SELECTED % of 26	UNSELECTED % of 83
MORTALITY	0	1.2
RECURRENT ULCER	0	4.8
SATISFACTORY	96.1	80.2
UNSATISFACTORY	3.9	19.8

TABLE XIIf

SERIOUS COMPLICATIONS	SELECTED 1 of 26 patients	%	UNSELECTED 16 of 83 patients	%
AFTERENT LOOP STASIS	0		2	
EFFERENT LOOP OBSTRUCTION	0		4	
JEJUNAL ULCER	0	3.9	4	19.8
SEVERE DUMPING & VOMITING	1		3	
SEVERE DIARRHOEA	0		3	

TABLE XIIf

POST-SURGERY SYMPTOMS	SELECTED % of 26	UNSELECTED % of 83
DYSPEPSIA	3.8	12
VOMITING	15.3	27.7
DIARRHOEA	0	9.6
DUMPING	7.5	22.9
WEIGHT		
LOSS	7.6	22.9
GAIN	0	0
FURTHER SURGERY	0	12

intensive medical therapy; 3 for severe dumping and vomiting and 3 for severe diarrhoea.

Post-Surgery Symptoms (Table XIIIf):

Considering all the symptoms elicited in these 2 groups it is evident that post-surgery symptoms were considerably greater in the unselected group.

The incidence of vomiting in the unselected group was appreciably higher than in the selected.

Vomiting and dumping had about the same incidence in the unselected group as the selected group. Serious symptoms were all higher in the unselected cases. Weight loss was common with this procedure and appreciable weight loss (up to 10%) was 3 times higher in the unselected than selected group.

II. HEMIGASTRECTOMY AND VAGOTOMY.

One hundred and four cases were submitted to this procedure. All except 3 were of the antecolic Polya variety with a Hofmeister valve. The remaining 3 had gastro-duodenal (Billroth I) anastomoses.

Sixty seven of this group were selected and the remaining 37 unselected.

Follow Up (Table XIIIa):

Sixty two of the 104 cases were followed up - 43 selected and 19 unselected; total follow up 59.6%.

Racial and Sex Incidence (Table XIIIb):

Females constituted only 15.4% of this group and 17.4% of all females operated on.

Acids (Table XIIIc);

Twenty eight of the 67 selected cases had post-operative acids studies; 14 of the 37 unselected patients had pre-operative acid secretory studies and 9 had post-operative acid studies.

The meanBAO and MAO were well below that of the selected group for this procedure. Analysing the secretory data of the unselected group, 11 (78.5%) of the 14 with pre-operative acid estimations could have had a vagotomy and drainage procedure. One patient with an excessive

... acid

HEMIGASTRECTOMY (ANTRECTOMY) + VAGOTOMY.

(TOTAL NUMBER 104).

TABLE XIIIa

	SELECTED	UNSELECTED
NUMBER	67	37
FOLLOWED UP	43	19
%	59.6	

RACIAL & SEX INCIDENCE.

TABLE XIIIb

NUMBER	EUROPEAN		COLOURED		BANTU	
	M	F	M	F	M	F
104	34	10	52	6	2	-
FOLLOWED UP 62	18	7	32	4	1	

ACIDS.

TABLE XIIIc

	No	SELECTED	No	UNSELECTED
		MEAN AND RANGE mEq/Hr		MEAN AND RANGE mEq/Hr
PRE-OP	67	BAO 9.4 (1.0-22.8) MAO 39.7 (21.5-62.7)	14	5.3 (10.5-20.8) 28.5 (17.0-52.9)
POST-OP	28	BAO 0.2 (0.0- 3.4) MAO 1.8 (0.0-12.9)	9	1.4 (0.0-9 .0) 3.7 (0.0-17.4)
% REDUCTION		BAO 97.9 MAO 95.5		BAO 73.6 MAO 87.0

acid secretion should have had a bigger resection than a hemigastrectomy according to our policy of selection. His post-operative acid output was 12.7 mEq/hr. (MAO) but no follow up data were available.

Total achlorhydria following histamine stimulation was encountered in 4 (10.8%) of the 37 post-operative secretory tests done, but the BAO was reduced to zero in no less than 32 (86.5%) of the 37 (histograms - Figs. XVII and XVIII).

The overall mean acid reduction attained with this procedure was 97.9% and 73.6% for the BAO and 95.5% and 87.0% for the MAO in the selected and unselected groups respectively.

Post-Operative Status (Table XIIId):

No mortality or recurrent ulceration was encountered with this procedure. Of the selected group, 95.3%, and of the unselected group, 94.7% could be classified as satisfactory.

Serious Complications (Table XIIIE):

Investigation of the 2 cases (5.3%) with unsatisfactory results in the selected group showed that 1 patient had severe afferent loop stasis, necessitating re-operation. Medical therapy was instituted in the other case for the

... vomiting

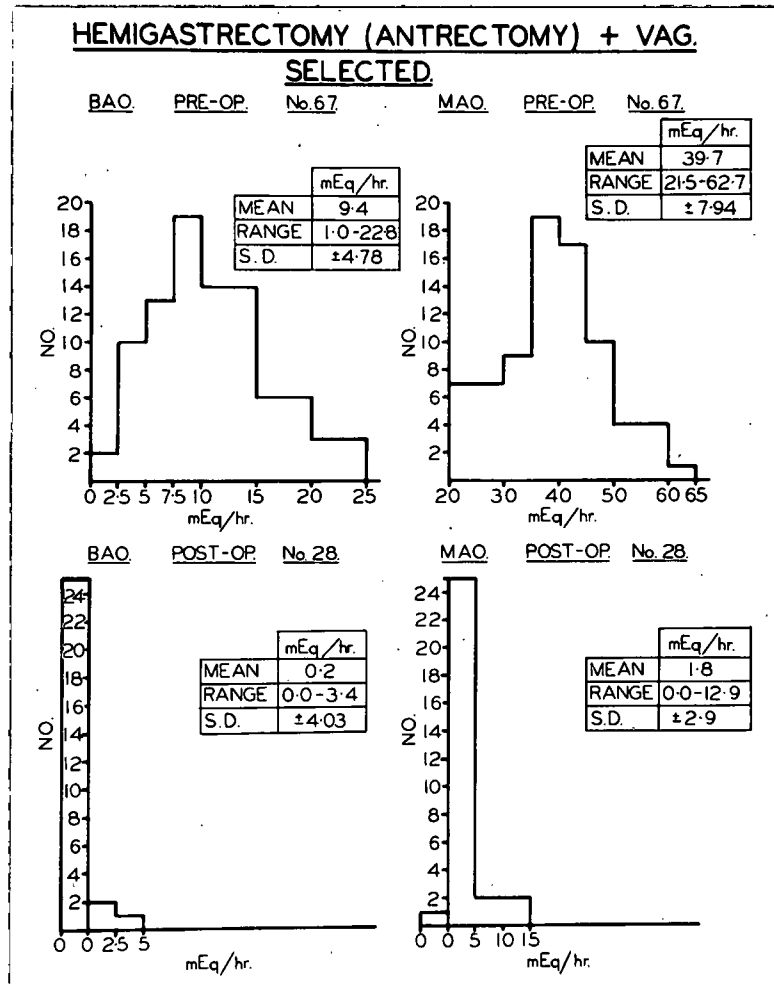


FIG. XVII.

Histograms of pre- and post-operative BAO and MAO in selected group of hemi-gastrectomy and vagotomy.

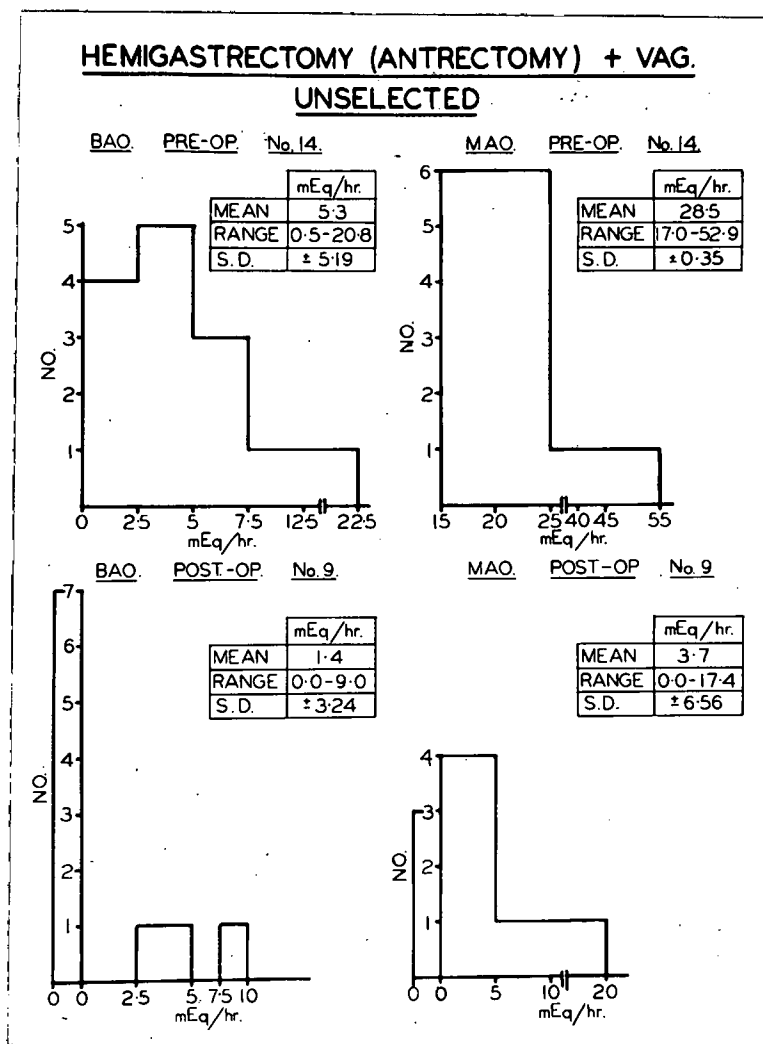


FIG. XVIII

Histograms of pre- and post-operative BAO and MAO in unselected group of hemigastrectomy and vagotomy.

HEMIGASTRECTOMY + VAGOTOMY

TABLE XIIIId

POST-OPERATIVE STATUS	SELECTED % of 43 patients	UNSELECTED % of 19 patients
MORTALITY	0	0
RECURRENT ULCER	0	0
SATISFACTORY	95.3	94.7
UNSATISFACTORY	4.7	5.3

TABLE XIIE

SERIOUS COMPLICATIONS	SELECTED 2 of 43 patients	%	UNSELECTED 1 of 19 patients	%
AFFERENT LOOP STASIS	2	4.7	1	5.3
DUMPING	1		1	
DIARRHOEA	0		1	

TABLE XIIIIf

POST-SURGERY SYMPTOMS	SELECTED % of 43 patients	UNSELECTED % of 19 patients
DYSPEPSIA	4.3	0
VOMITING	9.3	21.1
DIARRHOEA	11.6	15.8
DUMPING	9.3	31.6
WEIGHT		
LOSS	16.3	26.3
GAIN	7.0	5.3
FURTHER SURGERY	2.3	5.3

vomiting and dumping, and the response to date has been satisfactory.

The 1 case constituting the 5.3% poor result of the unselected group showed afferent loop stasis with diarrhoea and dumping. Corrective surgery has already been performed for this.

Post-Surgery Symptoms (Table XIII f):

Although the selected and unselected groups with this procedure were very similar in their overall satisfactory results, post-surgery symptoms were more marked in the unselected group. Dumping occurred in a bigger percentage of unselected cases, but in the majority it was mild. There was no appreciable difference in the incidence of diarrhoea in the 2 groups. Dyspepsia was infrequent. Weight loss was again common in these 2 groups but in 7% and 5.3% there was actually an increase in weight (up to 10%) for the selected and unselected groups respectively.

III. STANDARD GASTRECTOMY AND VAGOTOMY.

Twenty four of these procedures were performed. These were all selected and of the antecolic Polya-Hofmeister variety.

Follow Up (Table XIVa):

Seventeen of the 24 were followed up; a total follow up of 70.8%.

Racial and Sex Incidence (Table XIVb):

There was only 1 female in this whole group; all of whom were high acid secretors.

Acids (Table XIVc):

This procedure was reserved for patients with excessive gastric acid secretion as is indicated by the mean BAO of 16.6 mEq/hr. and a mean MAO of 63.2 mEq/hr. The BAO comprised the mean value for 23 patients. The one result (Case Report II) excluded from the mean BAO had a pre-operative value of well over 50 mEq/hr. and would have increased the mean BAO out of proportion for this small group of patients. The BAO in the 1 Bantu male in this group was 58.3% of the MAO and strongly suggestive of an unproven Zollinger-Ellison syndrome (Case Report III).

Post-operative acid secretory data were available in 9 of the 24 patients. Total achlorhydria was only

... encountered

STANDARD GASTRECTOMY & VAGOTOMY.

TABLE XIV (a)

NUMBER	24
SELECTED	24
FOLLOWED UP	17
% FOLLOW UP	70.8

TABLE XIV (b)

Racial & Sex Indicence.

	EUROPEAN		COLOURED		BANTU	
	M	F	M	F	M	F
NUMBER: 24	13	-	7	1	3	-
FOLLOWED UP: 17	11	-	3	1	2	-
% FOLLOW UP	70.8					

TABLE XIV (c)

Acids.

	NO.	SELECTED	
		Mean and Range mEq/hr.	
PRE-OP.	23	BAO	16.6 (4.0-28.4)(50+)
	24	MAO	63.2 (48.6-99.8)
POST-OP.	9	BAO	1.3 (0.0-9.3)
		MAO	3.1 (0.0-11.5)
% REDUCTION		BAO 92.2	MAO 95.1

encountered in 1 patient (11.1%) but virtual achlorhydria (MAO 0.1 mEq/hr.) was found in 5 (55.6%) (histogram - Fig. XIX).

The mean BAO and MAO were reduced by 92.2% and 96.5% respectively with this procedure.

Post-Operative Status (Table XIVd):

Only 1 (5.9%) of these cases could be classified as unsatisfactory.

Serious Complications (Table XIVE):

Corrective surgery was necessary in only 1 patient presenting with mild post-operative dyspepsia and post-prandial fullness, due to adhesive stomal obstruction. A feature of this case was the mildness of his symptoms (Case Report IV).

Post-Surgery Symptoms (Table XIVf):

It is of interest that post-operative symptoms in this group were infrequent and, when present, were of a mild nature.

Significant weight loss was present in 4 (23.5%) and in 1 (5.9%), and actual increases of over 10% occurred.

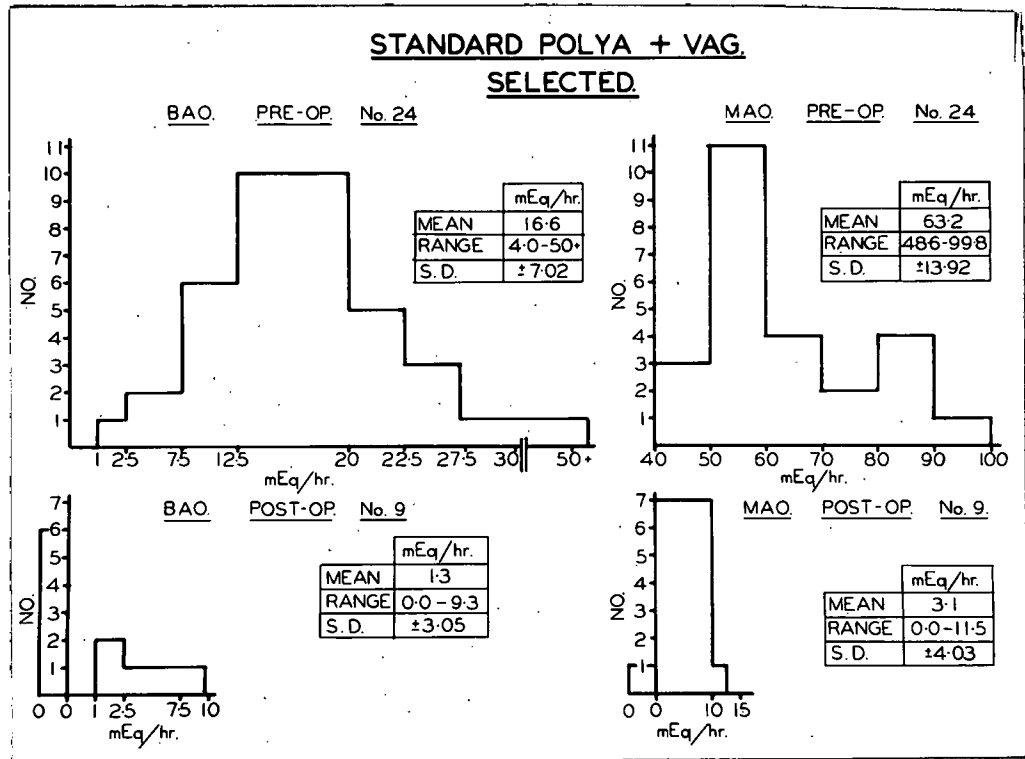


FIG. XIX.

Histogram of pre- and post-operative
BAO and MAO in selected group of
standard Polya gastrectomy with vagotomy.

STANDARD GASTRECTOMY & VAGOTOMY.

TABLE XIV (d)

POST-OPERATIVE STATUS	SELECTED % of 17.
Mortality	0
Recurrent Ulcer	0
Satisfactory	94.1
Unsatisfactory	5.9

TABLE XIV (e)

SERIOUS COMPLICATIONS	SELECTED % of 17.	%
Stomal obstruction	1	5.9

TABLE XIV (f)

POST-SURGERY SYMPTOMS	SELECTED % of 17
Dyspepsia	0
Vomiting	11.8
Diarrhoea	17.6
Dumping	11.8
Weight Loss	23.5
Gain	5.9
Further Surgery	5.9

IV. GASTRO-ENTEROSTOMY.

Fifty five gastro-enterostomies (gastro-jejunostomies) were done - 53 with vagotomy and 2 without vagotomy. All 55 were of the posterior short loop gastro-jejunostomy type.

A. GASTRO-ENTEROSTOMY WITH VAGOTOMY.

Of the 53 cases subjected to this procedure, 35 were selected and 15 unselected.

Follow-Up (Table XVa):

Thirty seven (69.8%) of this group were followed up.

Racial and Sex Incidence:

This is demonstrated by Table XVb, females contributing 26.4% in this group, or 17% of all females submitted to elective surgery in this series.

Acids (Table XVc):

Forty eight of 53 patients had pre-operative gastric acid secretory studies, constituting all the 38 selected cases and 10 of the 15 unselected cases. Acid secretory data was available in 24 of these post-operatively - 16 selected and 8 unselected.

Comparing the pre-operative acid output of the unselected group with that of the selected, the mean MAO of 40.4 mEq/hr. in the former group was appreciably higher

... than

GASTRO-ENTEROSTOMY + VAGOTOMY.

TABLE XVa

	SELECTED	UNSELECTED
NUMBER 53	38	15
FOLLOWED UP	27	10
% FOLLOW UP	69.8	

RACIAL & SEX INCIDENCE.

TABLE XVb

NUMBER	EUROPEAN		COLOURED		BANTU	
	M	F	M	F	M	F
53	19	17	13	3	1	-
FOLLOWED UP 37	15	13	8	1	-	-

ACIDS

TABLE XVc

	No	SELECTED	No	UNSELECTED
		MEAN AND RANGE mEq/Hr		MEAN AND RANGE mEq/Hr
PRE-OP	38	BAO 4.5 (0.7-12.4) MAO 25.5 (11.9-34.3)	10	5.6 (2.0- 7.8) 40.4 (36.5-48.0)
POST-OP	16	BAO 1.5 (0.0-4.4) MAO 6.0 (0.0-14.2)	8	3.9 (0.0-16.6) 19.5 (0.0-59.2)
% REDUCTION		BAO 66.7 MAO 76.5		BAO 80.4 (6) 30.4 (8) MAO 76.7 (6) 48.3 (8)

than that of the selected group, in whom the mean MAO was 25.5 mEq/hr.

The mean percentage acid reduction in the 2 groups was similar except for 2 patients in the unselected group who developed jejunal ulceration.

In 4 cases (3 selected and 1 unselected) the BAO was actually higher post- than pre-operatively. Vagotomy was complete in the 3 selected cases, but incomplete in the unselected case, on the basis of insulin testing.

Total achlorhydria was encountered in 1 case post-operatively and 3 cases had virtual achlorhydria (MAO about 0.1 mEq/hr.). The BAO was reduced to zero in 9 cases (histograms - Fig. XX).

In 19 cases the augmented histamine test was repeated post-operatively. The MAO reduction in:-

1 case	was	between	20 - 30%
1	"	"	30 - 40%
2 cases	"	"	40 - 50%
2	"	"	50 - 60%
4	"	"	60 - 70%
2	"	"	70 - 80%
2	"	"	80 - 90%
5	"	"	90 - 100%

From this it is seen that in the majority of cases (78.9%) the percentage reduction of the MAO was over 50%. The insulin test showed that the vagotomies were complete

... in all

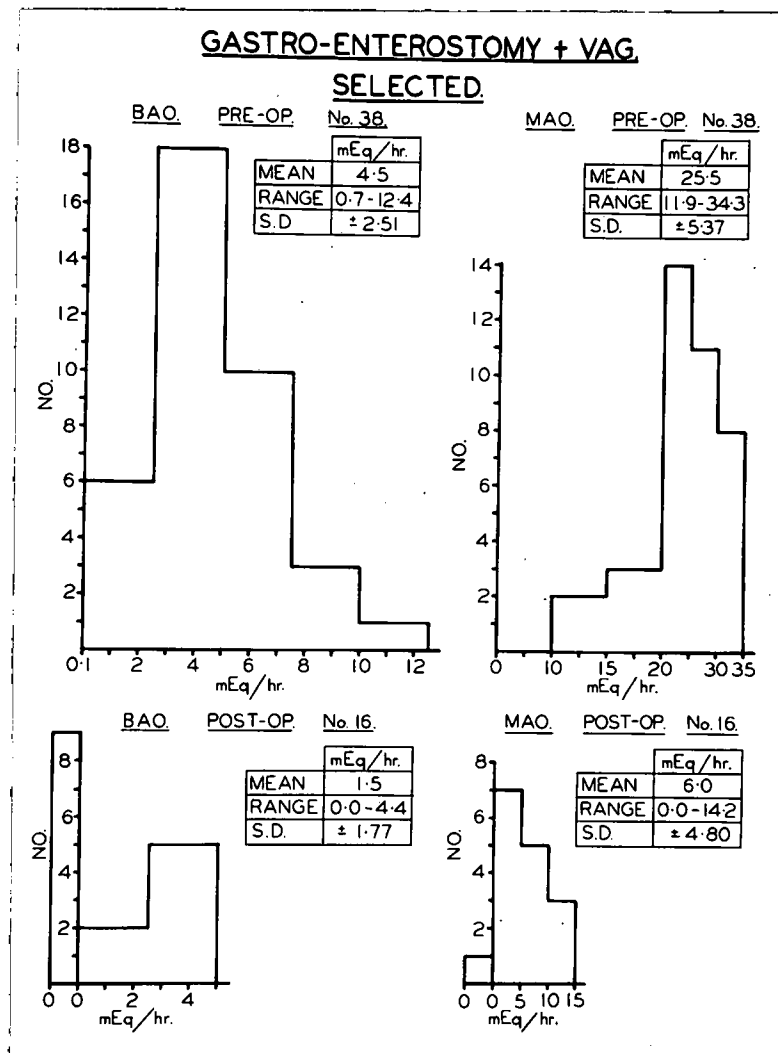


FIG. XX.

Histogram of pre- and post-operative
BAO and MAO in selected group of
gastro-enterostomy with vagotomy.

in all the cases (21.1%) where the reduction in the MAO was less than 50%.

Acid trends following gastro-enterostomy and vagotomy:-

The augmented histamine test was performed on more than one occasion on 17 patients post-operatively. The periods of investigation for the different groups of patients are shown in Fig. XXI. It is noted that in all groups the MAO diminished either progressively or diminished and then remained at a constant level of secretion. In one case, where the vagotomy was incomplete, the MAO increased above pre-operative level and then remained constant at the level of hypersecretion.

Post-operative Status (Table XVd):

There was no mortality with this procedure. Jejunal ulceration occurred in 2 patients, both in the unselected group, giving a 20% recurrent ulceration rate for the unselected group compared to 0% for the selected group, with an overall recurrent ulceration rate of 5.4% for gastro-enterostomy with vagotomy.

Of the 27 selected cases followed up post-operatively, 96.3%, and of the 10 unselected cases, 80% could be classified as satisfactory.

... Serious

MAXIMAL ACID OUTPUT AFTER VAGOTOMY AND DRAINAGE.

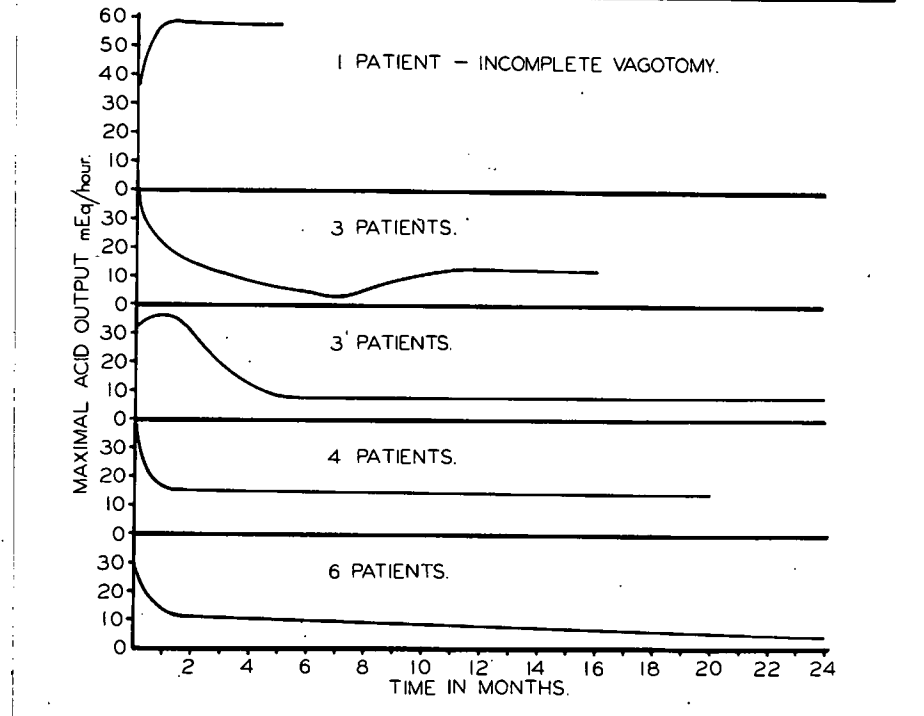


FIG. XXI.

GASTRO-ENTEROSTOMY + VAGOTOMY.

TABLE XVd

POST-OPERATIVE STATUS	SELECTED % of 27 patients	UNSELECTED % of 10 patients
MORTALITY	0	0
RECURRENT ULCERATION	0	2
SATISFACTORY	92.6	80
UNSATISFACTORY	7.4	20

TABLE XVe

SERIOUS COMPLICATIONS	SELECTED 1 of 27 patients	%	UNSELECTED 2 of 10 patients	%
AFFERENT LOOP OBSTRUCTION	1		-	
DYSPEPSIA	1	7.4	1	20
MELAENA	-		1	

TABLE XVf

POST-SURGERY SYMPTOMS	SELECTED % of 27 patients	UNSELECTED % of 10 patients
DYSPEPSIA	11.1	40
VOMITING	18.5	20
DIARRHOEA	18.5	10
DUMPING	11.1	0
WEIGHT:		
LOSS	0	10
GAIN	0	0
FURTHER SURGERY	3.7	20

Serious Complications (Table XVe):

In the whole group submitted to gastro-enterostomy and vagotomy, only 4 patients were classified as unsatisfactory; 2 cases (7.4%) in the selected group and 2 cases (20%) in the unselected group.

Investigating the post-operative complaints in these cases, it was found that:-

- (i) One of the selected cases had intractable dyspepsia and bile vomiting, necessitating re-operation (Case Report V), and the other had recurrence of dyspepsia (Case Report VI),
- (ii) The 2 unselected cases constituting the 80% poor results of this group both developed jejunal ulceration (Case Report VII).

Post-Surgery Symptoms (Table XVf):

Analysis of the individual symptoms encountered post-operatively showed that these occurred more frequently in the unselected group, but the number of patients in this group was small. Diarrhoea was somewhat higher in the selected group but not severe in either group. Mild dumping occurred infrequently and was slightly higher in the selected group. Weight loss was not encountered, except in 1 patient (10%) of the unselected group.

... B. Gastro-Enterostomy

B. GASTRO-ENTEROSTOMY WITHOUT VAGOTOMY:

Two patients were submitted to this procedure, one selected and one unselected.

Follow Up:

Both cases were followed up post-operatively; in both instances the period of follow up was relatively short.

Acids:

Both patients were elderly females. Pre-operatively the acid output for the selected case was BAO 0.0 mEq/hr. MAO 8.3 mEq/hr. Post-operatively the BAO was 1.0 mEq/hr. and MAO 4.5 mEq/hr. The acid output in the unselected case pre-operatively was BAO 11.7 mEq/hr. and 31.5 mEq/hr. for the MAO. Acid values could not be repeated post-operatively as this patient developed a coronary thrombosis.

Post-operative Status:

Both cases were satisfactory with no recurrence of pre-operative symptoms or post-operative sequelae.

V. PYLOROPLASTY.

This procedure was done in 25 cases - 24 with vagotomy, 1 without vagotomy. All the pyloroplasties were of the Heinecke-Mickulicz type.

A. PYLOROPLASTY WITH VAGOTOMY.

Twenty four patients were submitted to this operation - 22 selected and 2 unselected.

Follow Up (Table XVIa):

Seventeen of the 22 selected and 1 of the 2 unselected cases were followed up: a total follow up of 90% for this procedure.

Racial and Sex Incidence (Table XVIb):

It is of interest that (i) females accounted for double the number of males in this group, and (ii) that of all females operated on in this series, 14.6% had a pyloroplasty and vagotomy.

Acids:

Pre-operative acid studies were carried out on all 24 patients. Table XVIc demonstrates the mean BAO, MAO and range of gastric acid secretion for both the selected and unselected cases. As there were only 2 cases in the unselected group, a statistical analysis of acid secretion in the 2 groups was not possible.

... Post-

PYLOROPLASTY & VAGOTOMY.

TABLE XVI (a)

Total Number 24.

	SELECTED	UNSELECTED
NUMBER	22	2
FOLLOWED UP	17	1
% FOLLOW UP	90	

TABLE XVI (b)

Racial & Sex Incidence.

NUMBER	EUROPEAN		COLOURED		BANTU	
	M	F	M	F	M	F
24	4	8	4	7	-	1
FOLLOWED UP 18	3	6	2	6	-	1

TABLE XVI (c)

Acids.

	No.	SELECTED	No.	UNSELECTED
		Mean & Range mEq/hr.		Mean & Range mEq/hr.
Pre-Op.	22	BAO 3.7 (0.0-11.6)	2	11.0 -
		MAO 22.0(10.0-35.3)	5	30.7
Post-Op.	16	BAO 1.2 (0.0-3.0)	1	0.5 -
		MAO 6.4 (0.5-12.5)		15.0
Mean % Reduction		BAO 67.6 MAO 70.9		-

Post-operatively, 16 of the 22 selected and 1 of the 2 unselected cases had acid studies. In 6 (37.5%) of the 16 selected cases, the BAO was reduced to zero but achlorhydria was not encountered following histamine stimulation (histogram - Fig. XXII). In 3 of these 16 patients the post-operative BAO was higher than pre-operatively, but an insulin test done in 1 of these indicated complete vagotomy, despite the slightly higher basal acid secretion.

Acids:

The mean BAO and MAO reduction with this procedure was 67.6% and 70.9% respectively. In none of these cases was the MAO reduced by less than 50%:

In 3	between 50 - 60%
" 6	" 60 - 70%
" 2	" 70 - 80%
" 4	" 80 - 90%
" 2	" 90 - 100%.

Post-operative Status (Table XVIId):

No mortality or recurrent ulceration occurred in this group. Of the 17 selected cases followed up, 15 (88.2%) were clinically satisfactory.

... Serious

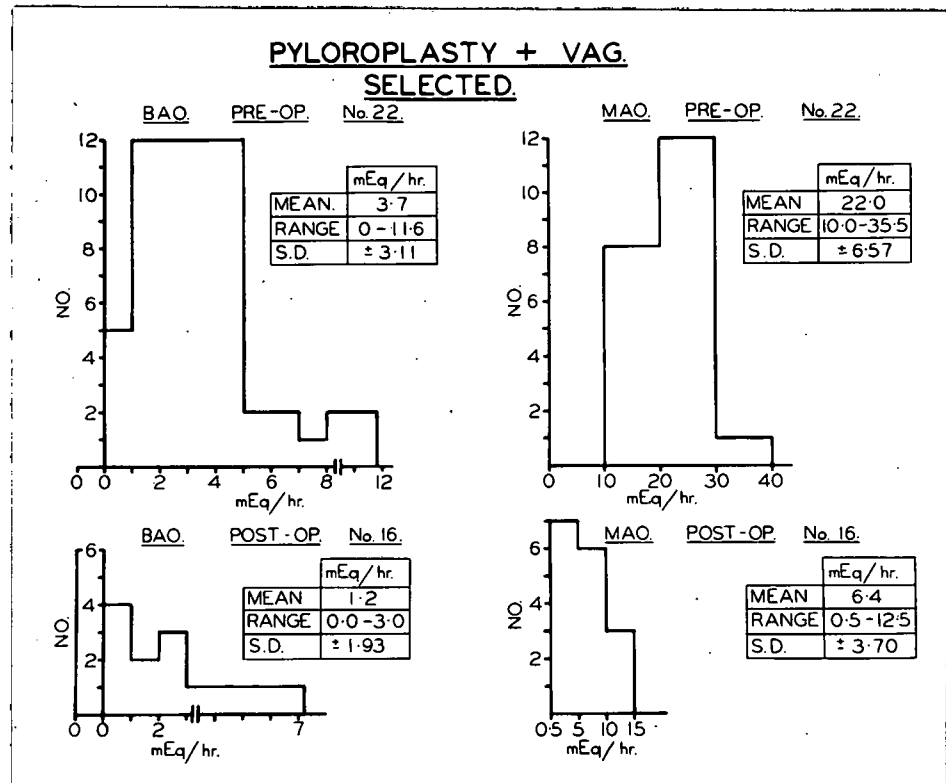


FIG. XXII.

Histograms of pre- and post-operative BAO and MAO in selected group of pyloroplasty and vagotomy.

PYLOROPLASTY & VAGOTOMY

TABLE XVI (d)

POST-OPERATIVE STATUS	SELECTED % of 17
MORTALITY	0
RECURRENT ULCERATION	0
SATISFACTORY	88.2
UNSATISFACTORY	11.8

TABLE XVI (e)

SERIOUS COMPLICATIONS	SELECTED SERIES 2 of 17 patients	%
Severe Dyspepsia	2	11.8
Dumping	1	
Diarrhoea	1	

TABLE XVI (f)

POST-SURGERY SYMPTOMS (SELECTED) 17 patients	%
Dyspepsia	17.6
Vomiting	6.0
Diarrhoea	28.0
Dumping	11.8
Weight Loss	0.0
Weight Gain	0.0
Further Surgery	0

Serious Complications (Table XVIe):

The remaining 2 patients (11.8%) constituted the unsatisfactory results. Investigation of these 2 patients showed that vagotomy had been complete, pyloroplasty adequate, and no radiological or gastroscopic evidence of duodenal or gastric ulceration was present. Despite this, a recurrence of their previous ulcer dyspepsia was the really troublesome complaint. These cases did not manifest the symptoms of post-surgery sequelae such as dumping, diarrhoea or vomiting. Both eventually settled on symptomatic treatment and superficial psychotherapy - Case Report VIII illustrates this problem.

Post-Surgery Symptoms (Table XVI f):

Analysing the individual symptoms encountered post-operatively in this group, dyspepsia occurred in 17.6% and diarrhoea in 28.0%, although diarrhoea requiring treatment was present in only 1 case (5.9%). Post-operative vomiting was not a troublesome feature and weight loss was not seen.

None of the patients in this group required corrective surgery.

B. Pyloroplasty

B. PYLOROPLASTY WITHOUT VAGOTOMY:

One patient only had this operation. The case selected was an elderly male with low acid secretion (BAO 2.6 mEq/hr., MAO 16.0 mEq/hr.) pre-operatively. The test could not be repeated post-operatively.

Post-operative Status:

His condition was satisfactory, with an actual increase in weight although the post-operative period was relatively short (6 months).

CHAPTER IV

EMERGENCY GROUP.

Forty one emergency procedures were carried out during the period of the study. Associated complications were present in 2 of the 41 patients:

- (i) Gastric ulcer associated with a duodenal ulcer,
- (ii) Stenosis and acute perforation associated with haemorrhage from a duodenal ulcer.

Polya gastrectomies were performed in all cases except 1, in whom a gastro-enterostomy and vagotomy was done.

Follow Up (Table XVIIa):

Seventeen of the 41 cases were followed up: a 41.5% follow up for this group.

Racial and Sex Incidence (Table XVIIb):

European males far out-numbered males and females of the other 2 racial groups.

Acids (Table XVIIc):

Acid secretory data were only available in 3 patients pre-operatively and in 10 post-operatively. Because of the small pre-operative number, no conclusions were reached.

Achlorhydria was present in 1 case post-operatively following histamine stimulation.

... Post-

EMERGENCY SURGERY.

TABLE XVII (a).

NUMBER	41
FOLLOWED UP	17
% FOLLOW UP	41.5

TABLE XVII (b).

Racial and Sex Incidence.

NUMBER	EUROPEAN		COLOURED		BANTU	
	M	F	M	F	M	F
41	22	5	8	5	1	-
FOLLOWED UP 17	8	1	4	3	1	-

TABLE XVII (c).

Acids.

	NO.	EMERGENCY MEAN & RANGE mEq/hr.
PRE-OP.	3	BAO 3.8 (3.0-4.4) MAO 31.9 (26.4-38.3)
POST-OP.	10	BAO 0.3 (0.0 - 1.8) MAO 2.3 (0 - 8.6)

Post-operative Status:

The mortality in this group of 41 patients was 17.1% (7 patients). These deaths all occurred in patients over 61 years of age. Fourteen cases over this age group were present in this series, the mortality thus being 50% for this age group, as compared to 0% for those 60 years and under.

To date, no recurrent ulceration has been encountered but the period of follow up is too short to evaluate this complication.

Fifteen (88.2%) of the 17 patients were satisfactory. The remaining 2 patients (11.8%) had moderate post-operative symptoms. Both had recurrence of dyspepsia, responding well to medical therapy.

CHAPTER V.

RELATED COMPLICATIONS IN DUODENAL ULCERATION.

ACUTE PERFORATIONS.

One hundred and four cases of acute perforations in duodenal ulcer were treated during the $3\frac{1}{2}$ year period. Ninety (86.6%) of these cases were treated by simple closure of the perforation. The remaining 14 (13.4%) were treated conservatively. In 2 instances the perforations occurred in patients on steroid therapy. In 1 case the perforation was due to a jejunal ulcer.

Follow Up (Table XVIIIa):

Fifty five (52.9%) of this group were followed up.

Racial and Sex Incidence (Table XVIIIb):

Females contributed only 7.7% (8 cases) of this group of patients. Of the rest, 57 (54.8%) were coloured, 38 (36.5%) European males, and 1 Bantu male. Males thus contributed 92.3% of this group.

Age Incidence:

The average age for European males was 44.2 years, whilst that for coloureds was 33.9, more than a decade earlier than the Europeans.

Acids:

Sixty eight of the 104 patients had gastric acid

... estimations

ACUTE PERFORATIONS IN DUODENAL ULCERATION.

TABLE XVIII (a)

NUMBER	104
FOLLOWED UP	55
% FOLLOW UP	52.9

TABLE XVIII (b)

Racial and Sex Incidence.

NUMBER	EUROPEAN		COLOURED		BANTU	
	M	F	M	F	M	F
68	38	4	57	4	1	-

TABLE XVIII (c)

Acids.

NUMBER	MEAN & RANGE mEq/hr.	
67	BAO	7.1 (0 - 39.2)
68	MAO	32.6 (10.4-99.8)

estimations following their perforations. The mean BAO, MAO and range of gastric acid secretion is shown by Table XVIIIc. In 15 (22.1%) cases the BAO exceeded 10 mEq/hr. with the highest up to 50 mEq/hr. Ten (14.7%) of these 15 cases had a BAO:MAO ratio greater than 40%.

Post-operative Status:

Of the 90 cases that were treated surgically, none died post-operatively. Two patients (1.9%) of the 14 treated conservatively were admitted in a moribund state and died before adequate resuscitation could make surgery possible. The other 12 cases treated conservatively recovered, and in 2 of these subsequent pelvic abscesses had to be drained, and in another a subphrenic abscess was drained.

Subsequent elective surgery was performed in 38 (55.9%) of 68 patients in this group of 104.

Of the 55 cases followed up, 4 (7.3%) of the 17 who did not require elective surgery following their perforations are being observed for moderate duodenal ulcer symptoms.

RECURRENT ULCERATION:

Thirty one cases of recurrent ulceration were investigated during the $3\frac{1}{2}$ year period under review. Six of these occurred in patients where the primary procedure was performed within the period of the study. All 6 cases occurred in the unselected group of patients - 2 following gastro-enterostomy and vagotomy, and 4 standard gastrectomy. The over-all incidence of jejunal ulceration in 380 elective procedures in this series was 1.6%. If this incidence is calculated only for the 186 unselected cases, it was 3.2%.

Acids:

Table XIX demonstrates the mean acid output in the 6 patients who developed this complication.

Two of the 6 jejunal ulcers occurring in patients of this series had pre-operative acid studies performed and in both an unselected surgical procedure was performed (Case Reports I and VII).

TABLE XIX

JEJUNAL ULCERATION.

ACIDS.

	No.	Mean and Range mEq/hr.
PRE-OP.	6	BAO 9.7 (5.6-16.6)
		MAO 30.1 (17.1-59.2)
POST-OP.	2	BAO 0.4 (0 - 0.7)
		MAO 5.2 (1.6 - 8.8)

Pre- and post-operative acid values shown
above are those before and after re-operation.

RE-OPERATIONS:

Forty four procedures were carried out for post-surgery sequelae in this period. Sixteen of these were for complications in patients where the primary intervention was done within the $3\frac{1}{2}$ year period - 6 being for jejunal ulceration. Two of the 6 cases of jejunal ulceration followed gastro-enterostomy and had subsequent re-gastrectomies; in both the vagotomies were incomplete. Initially, of the other 4 cases who developed this complication following standard Polya gastrectomy, 2 had re-gastrectomy plus vagotomy and 2 had only transthoracic vagotomies performed. All 6 were in the unselected group of patients.

Of the remaining 10 cases, 4 had conversions of a previous Polya gastrectomy to a Billroth I anastomosis for gross dumping, and 6 had re-operations for afferent and efferent loop syndromes. Five of the latter were for afferent loop obstruction, of whom 3 had Roux-en-Y procedures, 1 an entero-anastomosis and 1 case a Pantaloon procedure. The remaining case had stomal obstruction due to adhesions, which were freed.

ZOLLINGER-ELLISON SYNDROME.

Two cases of this syndrome were seen during the 3½ year period under review. Both were Bantu females, aged 51 and 22 years. One of these cases was reported in detail (Marks et al, 1961; Grossman et al, 1961). The other case presented as a haematemesis, had an emergency gastrectomy, and a large penetrating duodenal ulcer and tumour deposits in the liver were found. The histology of the hepatic nodules was identical with that found in the previous case.

Acids (Table XX):

Pre-operatively, only 1 case had gastric acid studies (Marks et al, 1961) and a Zollinger-Ellison syndrome strongly suspected, and could be considered as a selected case. Post-operatively the second case had repeated augmented histamine tests performed. The BAO:MAO ratio in both instances was over 60, the BAO actually being slightly higher in Case 2 than the MAO (Table XX - Case 2). Following anticholinergic therapy, both the BAO and the MAO were reduced by less than 50% in this case.

... Post-

TABLE XX.

ZOLLINGER - ELLISON SYNDROME.

(Total number 2).

CASE 1	ACIDS mEq/hr.		BAO:MAO RATIO
PRE-OP.	BAO	MAO	61.1
	20.7	33.7	

CASE 2	ACIDS mEq/hr.		BAO:MAO RATIO
	BAO	MAO	
POST-OP.	24.2	24.0	100.8
PROBANTHINE	14.0	12.8	109.4
% REDUCTION	42.2	46.7	
FOLLOWING DXR	0	0.6	

DXR = Radiotherapy

Post-operative Status:

The first case died post-operatively. The second case developed a jejunal ulcer 3 weeks post-operatively with acute exacerbations of her symptoms, suggesting a perforation. Following this, a course of radiotherapy to the gastric remnant was given with improvement in her general condition and a progressive decrease of gastric acid secretion to virtual achlorhydria (Bank et al - unpublished data).

GASTRIC BIOPSIES:

Sixteen gastric biopsies were done on post-operative patients at varying periods after surgery. Dyspepsia was present in 6 patients, the other 10 cases being absolutely symptom free.

Technique:

All specimens were taken with a Crosby capsule (Fig. XXIII).

After sucking 2 nupercaine lozenges, the Crosby capsule is inserted manually past the epiglottis from where it passes quite easily into the stomach on swallowing. Once the capsule is in the stomach, the patient is screened as for the augmented histamine test, the capsule positioned and the tube fixed to the side of the face. The patient is then placed comfortably in the supine position on a couch, the biopsy taken by sucking vigorously on the attached polythene tube with a 20 ml. syringe. Once the operator is sure that the capsule has closed, it is withdrawn, the biopsy specimen removed and prepared for histology.

Type of Operation:

Of the symptom free 10 patients investigated, 5 had standard Polya gastrectomies, 1 without a Hofmeister valve, 2 had standard Polya gastrectomy and vagotomy, and 3 hemigastrectomy and vagotomy.

... Of the



FIG. XXIII

"Crosby Capsule".

TABLE XXI.

GASTRIC BIOPSIES.
(Total Number 16)

No.	Operation.	Symptoms.	Post-op. Acids		Biopsy	Period since Surgery.	
			meq/hr.			Yrs.	Mths
			BAO	MAO			
1.	Stand.Poly.Gastr.	Nil	4.6	12.7	Normal	1	2
2.	" " "	"	-	-	Superficial Gastritis	-	9
3.	" " "	"	-	-	" "	1	7
4.	" " "	"	0	0	" "	1	1
5.	" " " without valve.	"	0	0.1	Atrophic "	-	10
6.	St.Gastr. + Vag.	"	0	1.6	Superficial "	1	10
7.	" " " "	"	14.9	17.3	" "	2	1
8.	Hemigastr. + Vag.	"	0	0.1	Atrophic "	-	11
9.	" "	"	0	0.1	Gastric Atrophy	1	1
10.	" "	"	0	0.1	Superficial Gastritis	1	-
11.	St. Polya	Dyspepsia	0	0	Normal	3	2
12.	" "	"	0	0	Superficial Gastritis	2	2
13.	" "	"	-	-	Atrophic "	6	-
14.	" "	"	6.4	8.3	Superficial "	2	5
15.	G-E + Vag.	"	1.4	4.3	Normal	2	5
16.	" " "	"	0	0	Superficial Gastritis	-	6

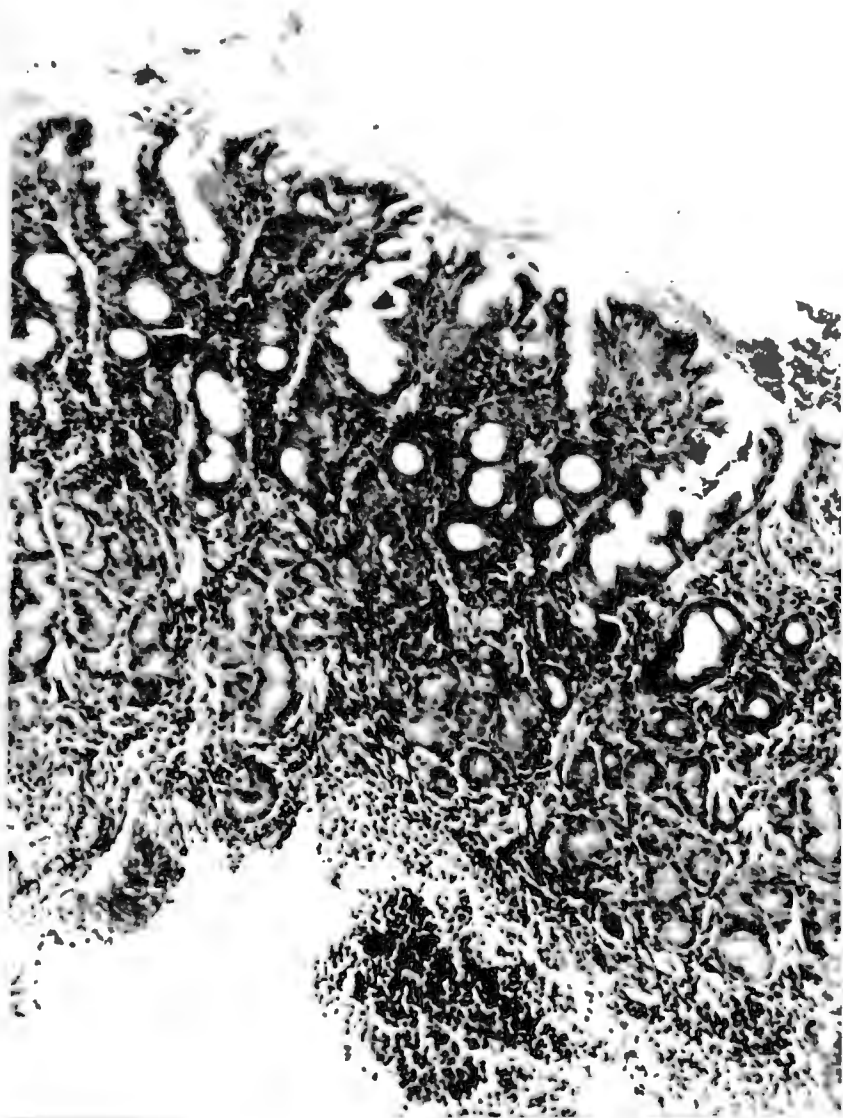


FIG. XXIV.

Atrophic gastric mucosa - low power:
gastric glandular layer is thin with
inflammatory cell infiltration.



FIG. XXV.

Atrophic gastric mucosa - high power:
abnormal and thin gastric glandular
layer plus inflammatory cell infiltration.

Of the 6 patients without symptoms of dyspepsia, 4 had standard Polya gastrectomies and the remaining 2 gastro-enterostomies with vagotomies.

Period since Surgery:

This varied from 6 months to 6 years post-operatively.

Acids (Table XXI):

Thirteen of these 16 patients had post-operative gastric acid estimations, of which 4 had total achlorhydria and another 4 virtual achlorhydria (MAO 0.1 mEq/hr.).

Biopsy Results:

Thirteen (81.2%) of the 16 patients had evidence of post-operative gastritis (9 superficial gastritis, 3 atrophic gastritis and 1 gastric atrophy). The remaining 3 biopsies were completely normal.

Analysing these results in the dyspeptic and non-dyspeptic patients, no appreciable histological differences were found. Neither the post-operative acid output nor the length of post-operative period seemed to have any relevant influence on biopsy results.

Figs. XXIV and XXV show typical histology of atrophic gastritis encountered in these cases.

BLOOD GROUPS IN DUODENAL ULCERATION:

It is generally accepted that the incidence of duodenal ulcer is 1.4 times greater in blood group O than in other groups.

Blood groups were available in 248 patients of this series. The incidence for the various groups was:-

Group O	51.6%
Group A	32.9%
Group B	11.3%
Group A/B	3.6%

Racial and Sex Incidence:

Table XXII shows the racial incidence for the different blood groups in this series. Comparing this with the incidence of the different blood groups in the general population (Table XXIII), the over-all incidence of duodenal ulceration was 1.2 times greater with Group O than the incidence of Group O in the general population. Analysing this association of Group O with duodenal ulcer for the different racial groups, the incidence was 0.99 for Europeans and 1.6 for the coloured population.

Acids: (Table XXIV)

One hundred and twenty of the 248 patients had pre-operative acid studies. Calculating the mean acid output for

... the

TABLE XXII

BLOOD GROUPS IN DUODENAL ULCERATION.

GROUP	EUROPEAN		COLOURED		BANTU		TOTAL
	NUMBER	%	NUMBER	%	NUMBER	%	
A	48	38.1	36	30.5	-	-	84
EB	14	11.1	14	12.7	-	-	28
AB	5	2.0	4	1.3	-	-	9
O	59	46.8 (.99X)	64	54.2 (1.6X)	4	-	127
TOTAL	126		118		4		248

TABLE XXIII.

BLOOD GROUPS IN THE GENERAL POPULATION
FOR THE DIFFERENT RACIAL GROUPS

(Expressed in Percentages)

GROUP	A	B	AB	O
EUROPEAN	42	8	3	47
COLOURED	41	21	5	33
BANTU	29.5	19.5	5	46

Data supplied by Western
Province Blood Transfusion Service.

ACID OUTPUT IN INDIVIDUAL BLOOD GROUPS
FOR RACIAL GROUPS.

TABLE XXIV.

GROUP	No	EUROPEAN	No	COLOURED	No	BANTU
		Mean & Range mEq/Hr.		Mean & Range mEq/Hr.		Mean & Range mEq/Hr.
A	22	BAO: 5.4 (0.0-16.5) MAO: 34.2 (10.0-80.7)	19	8.1 (1.6-28.4) 34.8 (19.0-57.9)	0	-
B	7	BAO: 7.2 (0.8-16.3) MAO: 41.1 (30.2-76.5)	8	8.1 (2.6-14.7) 31.7 (21.7-57.4)	0	-
AB	2	BAO: - MAO: -	3	- -	0	-
O	19	BAO: 5.3 (1.3-16.7) MAO: 32.4 (3.1-85.8)	37	7.9 (0.0-22.8) 32.1 (8.3-56.3)	3	-

for the different blood groups, an appreciably higher mean BAO was noted in Groups A and O in the coloured patients, and an appreciably lower mean MAO for group B in the coloured group compared to the Europeans. No marked differences were seen in the acid secretory data for Group O in the two races.

ASSOCIATION OF GASTRIC AND DUODENAL ULCER:

Among the 421 cases who had elective and emergency procedures, 33 were associated with concomitant gastric disease.

One of these 33 patients had a non-differentiated sarcoma of the stomach and in another an associated leiomyoma of the stomach was present. The remaining 31 had associated gastric ulcers, one of these being found during an emergency gastrectomy.

The incidence of gastric ulcer associated with a duodenal ulcer in this series was 7.4%. This is an appreciably lower incidence than that found by other workers. Hurst and Stewart reported a 12% incidence (Hurst and Stewart, (1929), Wilkie 50% (Wilkie, (1926),
✓ x Tanner 25% (Tanner, (1954) and Johnson 25% (Johnson, (1957)).

Seventeen of these patients had pre-operative acid estimations with a mean BAO 5.5 mEq/hr. (range 0.6 - 12.0 mEq/hr.) and a mean MAO of 29.1 mEq/hr. (range 6.3 - 44.8 mEq/hr).

Comparing these figures with the mean BAO and MAO found in duodenal ulcer patients (Table III - mean BAO 6.7 mEq/hr., mean MAO 36.6 mEq/hr.), an appreciably lower MAO was present.

VAGOTOMY:

Vagotomy combined with another gastric procedure was performed in 205 cases:-

Hemigastrectomy with vagotomy	104
Standard gastrectomy with vagotomy ..	24
Gastro-enterostomy with vagotomy	53
Pyloroplasty with vagotomy	<u>24</u>
	205

The insulin test was performed in 38 of these patients:-

- (i) Drainage with vagotomy 19
(gastro-enterostomy + vagotomy 13
pyloroplasty + vagotomy 6)
- (ii) Gastrectomy with vagotomy 19
(hemigastrectomy + vagotomy 10
standard gastrectomy + vagotomy 9)

Results:

Thirty eight insulin tests were performed. Applying strict criteria to the interpretation of this test, 26 (68.4%) of the 38 tests showed vagotomy to be complete.

Analysing the remaining 12 cases, 4 (10.5%) were incomplete on all criteria. The remaining 8 (21.5%) tests were difficult to interpret. In some there was a satisfactory acid reduction, but incomplete if measured

.... electrometrically

electrometrically or vice versa. The main difficulty in this group was bile reflux making interpretation difficult. If this last group is classified as adequate vagotomy, then the incidence of incomplete vagotomies in this series was 10.5%.

PART III.

ANALYSIS OF POST-OPERATIVE STATUS.

TABLE XXV

PROCEDURE		MORT	%	JU	%	DYSPEPSIA				%	BILIOUS VOMITING				%	DIARRHOEA				%	DUMPING			%	FURTHER SURGERY	%	WEIGHT					
						++	%	+	%		++	%	+	%		++	%	+	%		++	%		%			++	%	+	-	--	%
PPLASTY + VAGOTOMY	S 17	-		-		2	11.8	1	5.9	17.6	-	-	1	5.9	5.9	1	5.9	4	23.5	29.4	-	-	2	11.8	11.8	-	-	-	2	1	-	-
	U 1	-		-		-		1	-			-		-					-		-		-		-	-	1	-		-		-
GASTRO- ENT. + VAGOTOMY	S 27	-		-		1	3.7	2	7.4	4.1	1	3.7	4	14.8	18.5	-	-	5	18.5	18.5	-	-	3	11.1	11.1	1	3.7	-	-	5	2	-
	U 10	-	-	2	20	1	10	3	30	4.0	-	-	2	20	20	-	-	1	10	10		-		-		2	20	-	-	2	1	10
STAND. GASTR.	S 26	0.9	-	-		-	-	1	3.8	3.8	1	3.8	4	15.3	15.3	-	-	-	-	-	-	-	2	7.5	7.5	-	-	-	-	4	2	7.6
	U 83	1	1.2	4	48	4	4.8	6	7.2	12.0	7	8.4	16	19.3	27.7	3	3.6	5	6.0	9.6	2	2.4	17	20.5	22.9	10	12	-	-	11	17	22.9
HEMIGASTR + VAGOTOMY	S 43	-		-		1	2.3	1	2.3	4.7	1	2.3	3	7.0	9.3	-	-	5	11.6	11.6	1	2.3	3	7.0	9.3	1	2.3	3	7.0	8	11	16.3
	U 19	-		-				-			-	-	4	21.1	21.1	1	5.3	2	10.5	15.8	1	5.3	5	26.3	31.6	1	5.3	1	5.3	3	7	26.3
STAND GASTR + VAGOTOMY	S 17	-		-		-	-	1	5.9	5.9	-	-	2	11.8	11.8	-	-	3	17.6	17.6	-	-	2	11.8	11.8	1	5.9	1	5.9	1	5	23.5
TOTAL	S 130	-		-		4	3.1	6	4.6	7.7	3	2.3	14	10.8	12.3	1	0.8	17	13.8	14.6	1	0.8	12	9.2	10.0	3	2.2	4	3.1	20	21	10
	U 113	1	0.9	6	5.3	5	4.4	10	8.9	13.3	7	6.2	22	18.5	24.7	4	3.6	8	7.0	10.6	3	2.7	22	19.4	22.1	13	11.5	2	1.8	16	25	22.1

S = SELECTED
U = UNSELECTED

380 Elective 0.3%
41 Emergency 17.1%

DYSPEPSIA }
VOMITING } ++ Severe (incapacitating)
DIARRHOEA }
DUMPING } + Moderate to mild

WEIGHT } ++ gained 10% or more
+ gained under 10%
- lost; under 10%
LOSS } -- lost; 10% or more

INCIDENCE OF POST-SURGERY SYMPTOMS.
(Expressed as percentages)

TABLE XXVI.

SYMPTOMS	PPLASTY + VAGOTOMY				GASTRO-ENT. + VAGOTOMY				STAND.		GASTR.		HEMIGASTR + VAGOTOMY				STAND.GASTR. + VAGOTOMY				TOTAL.			
	S		U		S		U		S		U		S		U		S		U		S		U	
	R	T	R	T	R	T	R	T	R	T	R	T	R	T	R	T	R	T	R	T	R	T	R	T
DYSPEPSIA	11.8	17.6	-	-	3.7	11.1	10	40	0	3.8	4.8	12	2.3	4.7	0	0	0	5.9	-	3.1	7.7	4.4	13.3	
BILIOUS VOMITING	0	5.9	-	-	3.7	18.5	0	20	3.8	15.3	8.4	27.7	2.3	9.3	0	21.1	0	11.8	-	2.3	12.3	6.2	24.7	
DIARRHOEA	5.9	29.4	-	-	0	18.5	0	10	0	0	3.6	9.6	0	11.6	5.3	15.8	0	17.6	-	0.8	14.6	3.6	10.6	
DUMPING	0	11.8	-	-	0	11.1	0	0	0	7.5	2.4	22.9	2.3	9.3	5.3	31.6	0	11.8	-	0.8	10	2.7	22.1	
FURTHER SURGERY	0		-		3.7		20		0		12		2.3		5.3		5.9		-		2.2		11.5	
WEIGHT LOSS	0		-		0		10		7.6		22.9		16.3		26.3		23.5		-		10		22.1	
WEIGHT GAIN	0		-		0		0		0		0		7		5.3		5.9		-		3.1		1.8	

S= SELECTED

U= UNSELECTED

R = % TROUBLESOME ENOUGH TO REQUIRE TREATMENT

T = TOTAL

ANALYSIS OF RESULTS IN ENTIRE GROUP AND DISCUSSION.

A composite analysis of the results obtained with various surgical procedures in the treatment of duodenal ulcer, both in selected and unselected groups, is shown by Tables XXV and XXVI.

Table XXV is an analysis of the post-operative status. It shows the number of patients subjected to each surgical procedure (selected and unselected), the number and percentage of severe and total post-operative symptoms encountered in individual procedures, and the total numbers and percentages of individual sequelae encountered in the selected and unselected groups.

Table XXVI indicates the comparative incidence of individual post-surgery sequelae encountered in different surgical procedures, both in the selected and unselected groups.

In discussing the results obtained in this series, constant reference will be made to these two Tables.

Having embarked on a policy of selective surgery in the treatment of duodenal ulceration, two comparable groups of cases - selected and unselected - have evolved.

... Realising

Realising that only $3\frac{1}{2}$ years have elapsed since the institution of this policy, and that this period is not long enough to reach final conclusions, it is nevertheless long enough to ascertain whether the results obtained justify the continuation of this policy of selection based largely on gastric acid secretion.

TOTAL RESULTS.

A. CLINICAL EVALUATION.

The percentage of satisfactory results in the selected groups was greater in all the operative procedures, apart from hemigastrectomy and vagotomy, where virtually the same results in the selected and unselected groups were obtained.

(a) The satisfactory results obtained in the selected group of standard gastrectomies (96.1%) compared favourably with the 92.3% obtained in a comparative series reviewed by Orr (Orr, 1962). The 19.8% unsatisfactory results in the unselected group of standard gastrectomies is perhaps greater than the 8-12.4% reported from other large centres (Tanner, 1959(a); Clark and Logie, 1962; Stammers, 1959). Illingworth (Illingworth, 1960) estimated that there was a hard core of 9.4% with persistent disabling symptoms after standard gastrectomy.

Of the 19.8% unsatisfactory results in our series, 25% were due to recurrent ulceration and one may postulate that a standard resection is inadequate in a patient with

... a high

a high acid secretion and a large stomach, as is demonstrated by Case Report I; about one-third were treated for severe dumping and a further one-third for severe bilious vomiting and diarrhoea. It may be that a standard resection is perhaps excessive in a patient with a small stomach (Case Report VIII). The majority of this unselected group of patients could have had a gastro-enterostomy and vagotomy, according to our policy of selection, with the possibility of preventing some of these complications.

(b) The high percentage of satisfactory results obtained with standard gastrectomy and vagotomy (94.1%) is of interest as it has been shown that the bigger the resection, the greater the morbidity. Tanner (Tanner, 1954) estimated the morbidity to be as high as 28.5%, of which 9.6% were severe, and Waterhouse and Thorn (Waterhouse & Thorn, 1960) gave a figure of 12%. If two-thirds of the stomach was resected, this incidence increased to 21%, compared to 9.7% if less than two-thirds of the stomach was resected. Not only is the patient subjected to standard gastrectomy with vagotomy exposed to the complications of a major resection, but also to those due to the vagotomy per se. The high incidence of satisfactory results in this group of

... hypersecretors

hypersecretors with this procedure in this series could perhaps be explained by the fact that the stomachs in these patients are bigger (Cox, 1952) and, despite a two-thirds to three-quarter resection, the gastric remnant may still be about the size of one-half of the stomach in a moderate or low secretor.

(c) The percentage satisfactory results obtained both in the selected (95.3%) and unselected groups (94.7%) submitted to hemigastrectomy and vagotomy were virtually the same, notwithstanding the fact that a certain percentage of the unselected group could have been subjected to a gastro-enterostomy and vagotomy. The results obtained in this series compare favourably with those obtained by other workers (Pollock, 1952, 86%; Herrington et al, 1959, 97%; Edwards et al, 1963, 93%).

(d) Comparing the results of the selected and unselected groups of patients submitted to gastro-enterostomy with vagotomy in this series, the difference is very obvious. Perhaps this comparison is not valid because of the small number constituting the unselected group, .
^/
nevertheless a 20% failure rate due largely to recurrent ulceration should be emphasised if this procedure is going to be performed indiscriminately. The success of

... this

this procedure depends on the completeness of the vagotomy and in unskilled hands may result in subsequent misery for the patient.

However, if gastro-enterostomy and vagotomy are done in normal or low secretors, satisfactory results (92.6%) can be anticipated even in unskilled hands, for even if the vagotomy is incomplete the development of jejunal ulceration may be unlikely. The percentage satisfactory results obtained with this procedure compares favourably with the 100% quoted by Orr (Orr, 1962) in a selected series.

Where gastro-enterostomy and vagotomy are performed as an unselected procedure, a wide variation of satisfactory results is quoted: 76% to 90.7% (Pollock, 1952; Tanner, 1959(a); Fegetter and Pringle, 1963; Holt and Lythgoe, 1961; Walters et al, 1957; Hoerr, 1953), with the present series (80%) being more or less similar.

(e) Pyloroplasty with vagotomy showed the highest

~~p~~ Percentage of unsatisfactory results (88.2%) amongst the selected groups of patients in this series. Despite the higher incidence of unsatisfactory results as compared to the other procedures in this series, it is nevertheless more favourable than the 15.3% obtained by

... Orr

Orr (Orr, 1962) in a comparable selected group, or the 2% to 17% obtained by other workers in unselected groups (Stempien et al, 1958; Hendry, 1961; Weinberg, 1963; Pollock, 1952; Tanner, 1959(a)).

It is speculated that the relatively high incidence of failures in this group was due to the unwise selection of the patient for operation rather than to faulty surgical technique. The 15.3% to 17.5% failure rate reported by Orr, Tanner and Stempien may be due to similar faulty selection of patients for surgery. One is perhaps inclined to offer patients this surgical procedure, which carries the least physiological disturbance, where the history is unconvincing and psychological factors may predominate, where radiology is indefinite or minimal and low acid secretion exists.

TABLE XXVII.

PERCENTAGE SATISFACTORY RESULTS IN SELECTED AND
UNSELECTED CASES WITH INDIVIDUAL PROCEDURES

PROCEDURE	SELECTED	UNSELECTED
STANDARD GASTRECTOMY	96.1	80.2
HEMIGASTRECTOMY WITH VAGOTOMY	95.3	94.7
STANDARD GASTRECTOMY WITH VAGOTOMY	94.1	-
GASTRO-ENTEROSTOMY WITH VAGOTOMY	92.6	80.0
PYLOROPLASTY WITH VAGOTOMY	88.2	-

B. MORTALITY:

Elective Group (Table XXVIII)

In this series of 380 elective cases, one patient died post-operatively; a mortality rate of 0.3%. This death occurred in the group of unselected standard gastrectomies. Acid secretory values showed that a gastro-enterostomy and vagotomy could have been performed, according to our policy of selection. As this mortality was directly related to dissection of a difficult duodenum, it could almost certainly have been prevented if selection was applied. This incidence compares favourably with 1.3% quoted by Orr (Orr, (1962) for all procedures where selection was applied on more or less similar criteria to ours. The mortality in this series for standard gastrectomy (0.9%) also compares favourably with the average of 4%-5% in average hands (Hoerr, 1958; Johnson, 1959). On the other hand, it may be as low as 1% in centres specialising in gastric surgery.

Figures quoted by other workers are:-

Capper and Welbourn, 1955	- 1.5%
Welbourn and Johnston, 1961	- 3.6%
Johnson and Orr, 1954	- 1.5%
Armstrong and Penick, 1960	- 1.8%
Palumbo et al, 1960	- 4.0%
Tanner, 1959(a)	- 2.2%

... As no

As no deaths occurred with any of the other procedures, our mortality figures are very gratifying and compare well with the averages quoted for collective series, viz. 2.6% for vagotomy and antrectomy, 0.65% for gastro-enterostomy with vagotomy, and 0.6% for pyloroplasty with vagotomy (Welbourn and Johnston, 1961).

From these figures it can be seen that elective gastric surgery has become very safe in competent hands.

Emergency Group (Table XXVIII)

Seven of the 8 deaths reported in this series occurred among the emergency procedures; a mortality rate of 17.1%. The average age of these 7 cases was 74.6 years, with a range of 61 to 86 years. Two of these 7 cases had added surgical procedures which might have been a contributory factor in the subsequent mortality.

As seen in the elective group, above, surgery in duodenal ulceration has become remarkably safe. Our data shows that even emergency surgery is equally safe (0%) in patients under 60 years of age. However, this does not apply to those cases over 60, in whom the mortality reached the alarming figure of 50%. It follows that it is infinitely more hazardous to temporise with medical

... treatment

treatment in the elderly, despite the prevailing tendency to believe that these patients are less suitable candidates for elective surgery. Should emergency surgery be necessary in the elderly, it would appear unwise to do more than is absolutely necessary to control the emergency. Emergency surgery carries an appreciably higher death rate than elective surgery - 10% (Schnug et al, 1962). Avery Jones quotes a mortality rate of 10% for patients under 60 years, and 25% for those over 60 undergoing emergency surgery for haemorrhage (Jones, F.A., 1961).

TABLE XXVIII.

M O R T A L I T Y .

JAN. 1960 - JUNE 1963.

	AGE IN YRS.	NUMBER	OP. MORTALITY	
			No.	%
ELECTIVE	-	380	1	0.3
EMERGENCY	< 61	27	0	0
	> 61	14	7	50

C. RECURRENT ULCERATION.

The 6 jejunal ulcers encountered in this series all occurred in the 113 unselected cases followed up; an incidence of 5.3% compared to 0.0% for the 130 patients in the selected group. Orr, 1963, quotes a recurrent ulcer rate of 0.73% in his series.

Analysing the recurrence rate in the unselected group for the different procedures, it may be seen that of the 10 unselected cases submitted to gastro-enterostomy and vagotomy, 20% developed jejunal ulcers. This percentage is perhaps excessive because of the small number in this group, as it constitutes only 2 patients. Both cases had this procedure because of technical difficulties; in one the pre-operative acid secretory values were available (Case Report VII) and in both the vagotomies were incomplete. In both cases the post-operative acid values were well within the range usually encountered with this complication (Sircus, 1960; Bruce et al, 1959; Marks and Bank, 1963).

A widely varying incidence of recurrent ulceration with this procedure is quoted in the literature - from 0.8% to 13.3% (Holt, 1959; Fegetter, 1959; Burge, 1959;

... Hoerr

Hoerr, 1959; Edwards et al, 1960; Fegetter and Pringle, 1963; Walters and Mobley, 1957; Holt and Lythgoe, 1961).

The 4.8% jejunal ulcer incidence encountered in the 83 unselected standard gastrectomies is somewhat higher than the 0.4% to 2.2% range quoted in the literature (Palumbo and Sharpe, 1960; Capper and Welbourn, 1955; Brookes et al, 1960; Welbourn and Johnston, 1961;) but very similar to the 4.5% quoted by Welch and Rodkey in 1963.

Acid values available in only one of these cases pre-operatively showed this patient to be a hypersecretor (BAO 20.0 mEq/hr., MAO 56.0 mEq/hr. - Case Report I). Allowing for a 60-80% acid reduction with standard gastrectomy, the post-operative acid values would still have been within the jejunal ulcer range. Vagotomy was therefore indicated in addition. This was done subsequently for a jejunal ulcer, with satisfactory results.

No recurrent ulcers were encountered with the other procedures, viz. pyloroplasty with vagotomy, hemi-gastrectomy with vagotomy and standard gastrectomy with vagotomy. The absence of recurrence in the pyloroplasty with vagotomy group may be due to the fact that these cases were all low secretors in the first instance, and

... with a

with a complete vagotomy the probability of recurrent ulceration is low.

The absence of recurrent ulceration in patients in whom resection and vagotomy were carried out is not surprising since both the antral and the vagal factors acting on the parietal cell mass are attacked, and a low incidence therefore is to be expected. This is in keeping with the experience of other workers: 0.6% (Edwards et al, 1963), 0% (Palumbo and Sharpe, 1960), and 0.4% (Herrington, 1960).

It is stressed that it is as yet too early to make any claims about recurrent ulceration in this series. Suffice it to say that Ian Orr reports excellent overall results with only 1% recurrence in patients followed up for 10 years or longer, and that Kay has reported equally good results after a somewhat shorter follow up period. From our post-operative acid studies we are prepared to predict that our recurrent ulcer rate will not exceed those reported by Kay or Orr. Bank (personal communication) has shown that the acid output tends to drop even lower with time, in the vast majority of patients, and he postulates that this is due to the development of gastritis following gastro-jejunal

... anastomosis

anastomosis, further protecting the patient from jejunal ulceration.

D. DYSPEPSIA.

This symptom was present in 7.7% in the selected group of patients, as compared to 13.3% in the unselected group, with only 3% and 4% respectively requiring treatment. The 3% severe dyspepsia present in the selected group was mainly due to bad selection of patients for pyloroplasty with vagotomy and gastro-enterostomy with vagotomy (Case Reports VI and VIII). So far in this series, no recurrence of the initial ulcer has occurred and no further surgery was necessary. It is possible, however, that more prolonged follow up may reveal a reactivation of the initial ulcer. Orr (1962) quotes an 8.9% incidence of similar symptoms in his series.

The standard gastrectomy group of patients comprised the bulk of the 4% with severe dyspepsia encountered in the unselected group. The 10% severe dyspepsia found in the unselected group of patients after gastro-enterostomy with vagotomy appears to be very high, but in fact constituted only 1 patient.

Although no gastroscopic or radiological evidence of an acute exacerbation of a previous ulcer or recurrent

... ulceration

ulceration in these patients was found, it is interesting to speculate why this symptom should occur. It may, of course, be due to a small ulcer missed during the follow up, which may manifest itself at a later date, or it could be due to ensuing gastritis. Gastric biopsies have shown that there is little difference in histological appearance between the dyspeptic and non-dyspeptic patients. However, some patients may react to gastritis with dyspepsia while others do not, analogous to the situation found in subjects with intact stomachs.

The question of gastritis causing post-operative dyspepsia is a difficult one to settle. Wolf (1957) has shown gastritis to be present in 50% of patients with symptoms post-operatively, and in the same percentage of patients without symptoms. Lees and Grandjean (1958) found severe changes in two-thirds of asymptomatic stomachs post-operatively. Bookus (1963) states that "changes are as common after operation among asymptomatic patients as among those with symptoms or signs of post-gastrectomy disorders. It can be concluded that diffuse mucosal abnormalities such as observed endoscopically or in biopsies are seldom if ever clinically significant."

... On the

On the other hand, one may postulate that dyspepsia is caused by an afferent loop distending after a meal, giving a feeling of fullness and perhaps vague discomfort. Another condition that should be kept in mind in investigating post-operative dyspepsia is functional dyspepsia. The history prior to surgery should be carefully analysed and compared to post-operative recurrent dyspepsia to exclude this difficult problem.

E. BILIOUS VOMITING.

This symptom was twice as common in the unselected as in the selected group. Therapy was only necessary in 2.3% of the selected group for this complication, as compared to 6.2% in the unselected group. The incidence of bilious vomiting in selected gastro-enterostomy with vagotomy was no less than in selected standard gastrectomy, or resection with vagotomy. Severe bilious vomiting in the unselected group was only found in the standard gastrectomy group.

The 3.7% incidence of this complication found in gastro-enterostomy with vagotomy in this series was more or less the same as the 4% quoted by Welbourn and Capper (1955), but exceeds the 0.5% quoted by Fegetter and Pringle (1963).

The 8.4% of severe bilious vomiting present in the unselected standard gastrectomy compared well with the 9.6% quoted by Welbourn and Capper (1955). The afferent loop syndrome has been the most frequent and troublesome post-operative complication encountered by Orr (1963) in a large series.

As the afferent loop is purely anatomical, it is

... difficult

difficult to account for the higher incidence of this symptom in the unselected series. One may speculate however that in the unselected group a higher percentage of patients had major resections, leaving a smaller gastric remnant and requiring smaller quantities of bile to produce this symptom.

F. DIARRHOEA.

This was encountered in 14.6% of selected cases and 10.6% of the unselected group. Although the incidence in the selected group was higher, only 1% of these cases was severe, as compared to 3.6% of the unselected group. This 1% of the selected group represents 1 patient with severe diarrhoea following a pyloroplasty with vagotomy. The 3.6% of the unselected group was found mainly following standard gastrectomy procedures. By and large, diarrhoea was not a troublesome feature at all in this series, and many of these patients will admit to more frequent bowel actions following surgery, but usually this was a welcome relief from their pre-operative constipation.

The 3.6% diarrhoea encountered in unselected subtotal gastrectomy corresponds with the experience of other workers (Welbourn and Johnston, 1961; Orr, 1963). The experience of Burge (1959), that diarrhoea occurred in 20% of patients following gastrectomy, and in 30% following gastro-enterostomy, was not substantiated in this series. Other workers put the incidence of diarrhoea following vagotomy at less than 8% (Fegetter, 1959;

... Holt

Holt, 1959; Fegetter and Pringle, 1963), with an average of 4%.

Just how many stools a day should be regarded as diarrhoea is not clear, neither has the character of such stools been considered. As stated, many patients on direct questioning will admit to 2 - 3 soft stools a day. A certain percentage will also admit to intermittent periods of loose, watery stools, not incapacitating them in the least. Many patients will describe the character of these soft stools as clay coloured, floating, and sometimes a bit malodorous. These should perhaps rather be regarded as mild forms of post-operative steatorrhoea and not diarrhoea. Vagotomy should not be regarded as the cause of these, for there are ample reasons to explain this without incriminating the vagotomy. It has been shown that by bypassing the pancreas, as happens in a gastro-jejunal anastomosis, that this organ is not functioning maximally (Butler, 1960), and for the same reason with some intestinal hurry occurring post-operatively, no proper mixing of gastric chyme and pancreatic secretions can occur, leading to some deficient utilisation of fat, another factor perhaps contributing to weight loss.

... Perhaps

Perhaps diarrhoea should only be noted as positive once this condition becomes severe enough to interfere with the patient's work or leisure. Those cases where the stools take on a steatorrhoeic character should possibly be separated from those with diarrhoea, the actual cause(s) investigated, and classified as a separate post-operative entity.

G. DUMPING.

Dumping occurred in 10% and 22.1% of the selected and unselected groups respectively, of which only 0.8% in the selected and 2.7% in the unselected groups were severe. This complication was not seen in vagotomy and drainage procedures in any severe form. Those requiring treatment all followed resection; standard gastrectomy and hemigastrectomy with vagotomy contributing all the cases with severe dumping in this series. This is in keeping with the findings of Holt (1959) and Weinberg (1963). Severe dumping was not encountered in the standard gastrectomy and vagotomy group, probably because a bigger gastric remnant is left behind, allowing for better mixing, and thus reducing the hypertonic solution to more isotonic levels.

In Orr's selected series (Orr, 1963), dumping was present in 10.7% of cases - 11% after vagotomy and resection, corresponding with the 9.3% encountered in this selected series following hemigastrectomy with vagotomy. Severe dumping following unselected Polya gastrectomy occurred in 2.4%, an incidence considerably less than the 12% quoted in Orr's series and 8% quoted

... by

by Welbourn and Capper (1955), and about the same as 1.2% quoted by Welch and Rodkey (1963).

In this series, no distinction was made between the early and late dumping syndromes, although those cases presenting with this symptom were investigated and had glucose tolerance curves done. In a few, oral hypoglycaemic agents were given. The results of these, however, fall outside the scope of this work. It was interesting to note that patients complaining of early dumping frequently ascribed their symptoms to milk and milk products and by avoiding these could ameliorate their discomfort.

H. WEIGHT LOSS OR GAIN.

Weight loss or gain in this series was estimated in percentages and an increase or decrease of 10% of ideal weight was considered significant.

Weight loss in the unselected group was more than double that of the selected group - 22.1% as compared to 10%. This difference could possibly be attributed to the large group of unselected standard gastrectomies performed in cases where vagotomy and a drainage procedure could have been done, because it was noticeable that weight loss became very evident in the groups where gastric resections were done. This feature was not observed with vagotomy and drainage procedures. On the other hand, weight increase was not more noticeable after vagotomy and drainage, despite the claims of some workers that this is one of the advantages of these procedures. There was also no difference in weight gain between the group with pyloroplasty and vagotomy, and those with gastro-enterostomy and vagotomy, although it is claimed by some authors that weight gain is better following a gastro-enterostomy than a pyloroplasty. The highest incidence of more than 10% weight loss among the selected

... groups

groups of patients was found in the standard gastrectomy with vagotomy group.

Amongst the unselected groups, this was found with hemigastrectomies with vagotomies, and standard gastrectomies. Where selection was applied in these 2 groups, weight loss was not worse than that claimed by other workers (Scott, 1960). These findings again could possibly be attributed to unnecessary resections.

Different workers use different criteria for estimation of weight loss. Anderson et al (1955) consider a loss of 10 lbs. below tabular weight of no significance. Sandweiss et al (1952) estimate weight loss in percentages, taking a gain or loss of 5 lbs. as their index, with Clark and Logie (1962), 14 lbs. as their criterion.

It is difficult to state what criterion should be adopted for the estimation of this post-operative sequela, because some weight loss in an obese patient with previous coronary heart disease may be beneficial, while on the other hand, a manual labourer who is unable to maintain his nutrition will have a serious drawback.

... In deciding

In deciding which procedure should be performed in various patients, therefore, serious consideration should be given to these socio-economic and physiological factors.

I. ACID SECRETION.

That surgery in duodenal ulceration is solely indicated on clinical grounds must be stressed, but that gastric acid secretory data are valuable additional knowledge is beyond dispute.

In hypersecretors, the chief problem is one of recurrent ulceration after surgery. This can be prevented by a collective attack on the vagal and antral phases of gastric secretion acting on the parietal cell mass. Pre-operatively armed with acid output values in this important group of patients, subsequent misery can be avoided and a high percentage of satisfactory results expected because of the fact that a subtotal resection in these patients will still leave them with an adequate gastric reservoir with which to maintain nutrition.

In moderate secretors, more leeway may be allowed and a choice of procedure is reasonable, depending on the experience of the surgeon in a particular technique and on the needs of the patient. On the other hand, too minor a procedure - like a gastro-enterostomy with vagotomy - must not be performed either, for with a failed vagotomy in these
... circumstances

circumstances only a 20-30% acid reduction can be expected (Gillespie et al, 1960), with the incidence of recurrent ulcer no less than in the hypersecretor group. This is therefore a difficult group in which to decide what is best for the patient, but with selection as laid down in the policy we follow, satisfactory results can be anticipated.

In low secretors, extensive resections are unnecessary and only increase the incidence of post-gastrectomy sequelae. It is well known that the bigger the resection, the bigger the incidence of unpleasant post-operative sequelae, such as dumping and malnutrition (Wells and MacPhee, 1954; Black and Rechnitzer, 1953). This group should therefore ideally have a gastro-enterostomy with vagotomy, for even with a failed vagotomy recurrent ulceration will be unlikely in these circumstances. Gastro-enterostomy with vagotomy are indicated in this group rather than pyloroplasty, because of the relatively poor results obtained with the latter procedure in this series.

Another valuable advantage of pre-operative acid estimations is that these may alert one to the possibility

... of the

of the presence of a Zollinger-Ellison syndrome. If the ratio of the pre-operative BAO:MAO is 60% or more, a non-beta cell pancreatic tumour should be seriously suspected and conscientiously searched for at surgery. This fact is well illustrated by the two cases described in this series.

The estimation of acid secretory levels post-operatively may serve as valuable aids in the investigation of post-operative complications. Bleeding occurring in these patients, with acid secretory levels in the recurrent ulcer range, despite the inability to demonstrate such a lesion radiologically, gastroscopically or otherwise, may be taken as proof of its presence and treated accordingly. On the other hand, bleeding in an achlorhydric patient would lead one to suspect some other cause, e.g. stitch ulcer, other gastro-intestinal pathology or a blood dyscrasia. From post-operative acid estimations done on patients presenting with troublesome post-operative sequelae, it would appear that the incidence of steatorrhoea and anaemia is higher in patients with total achlorhydria (Bank, and Marks, personal communication

1963). Why the incidence of steatorrhoea should be higher in these patients is unknown. It may be that acid is necessary for the splitting of fat and, if not available, fat cannot be absorbed. Anaemia in these patients could possibly be explained on the basis that the iron ingested cannot be converted to the ferrous salt which is the soluble and diffusable form due to the absence of hydrochloric acid. If this is so, then these complications can be expected to be less in the selected group of patients, as the incidence of achlorhydria was appreciably less in this group (Table XXIX).

The percentage acid reduction achieved with different surgical procedures in this series (Table XXX) is somewhat greater than that obtained by Gillespie and his associates (Gillespie et al, 1960). A certain margin of error must be expected in post-operative acid estimations because of escape of gastric acid through the stoma, and bile reflux neutralising a certain amount of gastric secretion.

An interesting phenomenon found in a few patients was that the post-operative BAO levels were higher than the pre-operative levels. These seemingly anomalous results

... were

TABLE XXIX

PERCENTAGE TOTAL ACHLORHYDRIA
WITH INDIVIDUAL PROCEDURES.

PROCEDURE	SELECTED	UNSELECTED
Gastrectomy	8.3	15.0
Hemigastrectomy with Vagotomy	7.6	33
Standard Gastrectomy with Vagotomy	11.1	-
Gastro-enterostomy with Vagotomy	0	0
Pyloroplasty with Vagotomy	0	-

TABLE XXX..

PERCENTAGE ACID REDUCTION WITH
INDIVIDUAL PROCEDURES

PROCEDURE	SELECTED		UNSELECTED	
	BAO	MAO	BAO	MAO
Standard Gastrectomy.	74	93.5	86	87.6
Hemigastrectomy with Vagotomy	97.9	95.5	73.6	87.0
Standard Gastrectomy with Vagotomy	92.2	95.1	-	-
Gastro-enterostomy with Vagotomy	66.7	76.5	80.4	76.7
Pyloroplasty with Vagotomy	67.6	70.9	-	-

were found only following vagotomy and drainage procedures. It is possible that this was due to technical errors; e.g. incomplete aspiration of the fasting gastric juice, or slow emptying of the stomach, or perhaps that the antral phase of gastric secretion predominated in these cases (Kay, 1961).

C O N C L U S I O N S .

CONCLUSIONS.

The results suggest that no single surgical procedure will suit all patients suffering from duodenal ulceration. Clinical evaluation of the individual patient remains the most important factor in deciding whether surgical intervention should be undertaken or not. Once surgery has been decided upon, additional knowledge of gastric acid secretion can direct the surgical approach most suitable for the individual patient, and better results may be obtained.

An analysis of the results over a $3\frac{1}{2}$ year period confirmed that selection of patients according to their acid secretion, as the basis for the type of operation to be performed, has undoubtedly improved the yield of satisfactory post-operative results and reduced the incidence of complications.

While indiscriminate standard gastric resections yielded relatively unsatisfactory results, it remains a good procedure where the indications are correct.

... Hemi-

Hemigastrectomy with vagotomy produced a consistently high percentage of satisfactory results in a large proportion of patients, and should perhaps be practised more often in the absence of acid secretory data.

In the 10-20% of patients with hypersecretion, resection alone will not be enough to prevent jejunal ulceration, and the addition of a vagotomy will probably procure the safety of these patients. A high percentage of satisfactory results can be obtained in these patients if they are carefully selected.

Performing gastro-enterostomy with vagotomy indiscriminately proved to be unsatisfactory. This was largely due to the fact that a 10% incomplete vagotomy rate may be anticipated and subsequently the association of acid hypersecretion and incomplete vagotomy led to a rapid jejunal ulcer recurrence. Occasionally this procedure is necessitated, due to technical difficulties, despite the knowledge that hypersecretion exists.

Pyloroplasty and vagotomy has not produced the expected good results in this series. This may be due

... to the

to the poor selection of patients for surgery. This procedure was often resorted to when chronic ulceration could not be demonstrated at surgery, and pyloroplasty had already been undertaken to explore the duodenal cap.

Jejunal ulceration can substantially be reduced and perhaps completely avoided with selection of cases according to their gastric acid secretion.

Serious diarrhoea following vagotomy was not experienced in this series, and the occurrence of this complication should not deter one from adding vagotomy where indicated. Diarrhoea did not occur appreciably more often following vagotomy than after standard resection.

Post-operative dyspepsia is a nebulous term and therefore difficult to assess. Nevertheless, some types of dyspeptic symptoms were encountered in many patients during the follow up period and these were found to be more frequent in the unselected group of patients.

Bilious vomiting can be reduced substantially by selective surgery but is no less prominent after gastro-

... enterostomy

enterostomy than after gastric resections. Unless the afferent loop can be avoided, it would appear that this symptom is bound to occur.

Serious dumping was not experienced in vagotomy and drainage procedures, but the incidence was appreciably less where selective resections were performed.

Appreciable weight loss only became evident where resections were performed. Just what percentage of weight loss should be considered as significant is difficult to assess, but that substantial weight loss is a serious handicap to a manual labourer, needing a high caloric intake, is obvious. Selective surgery can reduce the incidence of this complication appreciably by limiting the incidence of resections.

S U M M A R Y .

SUMMARY.

Selective surgery in chronic duodenal ulceration was started $3\frac{1}{2}$ years ago with the aim of establishing whether the early and late post-operative results of gastric surgery could be improved.

Three hundred and eighty patients with duodenal ulceration who were subjected to surgery have been analysed; 194 were operated on according to the policy of selection and 186 formed the unselected group.

Selection was undertaken on the basis of gastric acid secretion. The patients were divided into the categories of high, moderate and low secretors. A BAO of more than 10 mEq/hr. and MAO of more than 50 mEq/hr. was termed a high secretor; BAO of under 10 mEq/hr. and MAO of 35-50 mEq/hr. was a moderate secretor; BAO of less than 10 mEq/hr. and MAO under 35 mEq/hr. a low secretor.

The policy of selection accepted was standard resection and vagotomy for high secretors, standard gastrectomy or hemigastrectomy with vagotomy for

... moderate

moderate secretors, and vagotomy and drainage for low secretors.

The unselected group of patients comprised those in whom acid secretory data was not available or those with acid secretory data available but the indicated procedure not performed.

Acid output was measured by means of the augmented histamine test, which provides a measure of all three parameters controlling gastric acid secretion. BAO measures not only the nervous phase of gastric secretion, but also the antral or gastric phase. The MAO is a direct reflection of the parietal cell mass.

The results in the selected and unselected groups are compared according to incidence of satisfactory results obtained, the occurrence of jejunal ulceration, the incidence of post-operative dyspepsia, bilious vomiting, diarrhoea, dumping and weight loss. The selected group showed superior results in virtually all these parameters, except post-operative dyspepsia, where very little difference between the two groups was noticed. Jejunal ulceration only occurred in the unselected group.

... The results

The results obtained with each individual procedure in selected and unselected patients are shown and compared. Serious post-operative complications are pointed out and results analysed according to the above-mentioned parameters. Better results on each occasion were obtained in the selected patients in individual procedures. The highest percentage unsatisfactory results for selected patients were obtained with pyloroplasty with vagotomy, and for unselected patients with standard gastrectomy.

The physiology, pathophysiology and evolution of gastric surgery are discussed. The methods of doing the augmented histamine test, the insulin test and gastric biopsies are outlined.

Brief mention is made of acute perforations, blood groups in association with duodenal ulceration, the association of duodenal ulceration with gastric ulcer, and cases of Zollinger-Ellison syndrome encountered. The incidence of incomplete vagotomy and the number of this procedure performed are shown.

... In conclusion

In conclusion, it would appear that the results of gastric surgery in duodenal ulceration may be improved by selecting patients for surgery according to their acid output. While the period of follow up of $3\frac{1}{2}$ years may be too short for a final evaluation of results, there seems little doubt that a trend has been established, and that the policy of selection should be adhered to. The approach is a rational one and is ultimately dependant on the physiology of gastric secretion as it is known today.

A D D E N D U M A.

ADDENDUM A.

C A S E R E P O R T S .

I. N.M. Aet 35

History: Five year periodic post-prandial dyspepsia. Recent change in character of pain with radiation through to the back and associated symptoms of pyloric stenosis. Acute perforation 1 year prior to surgery. Three previous episodes of haematemesis and melaena.

Examination: Upper abdominal distension and visible peristalsis.

Investigations: Barium meal: dilated stomach with duodenal stenosis.

Acid secretion: BAO 20.0 mEq/hr.

MAO 56.0 mEq/hr.

Suggested operation: standard gastrectomy with vagotomy.

Operation: Two-thirds standard gastrectomy performed.

Operative findings: Pyloric stenosis with post-stenotic dilatation.

... Post-

Post-Operative: Exacerbation of symptoms 1 year after surgery. Regastrectomy performed to be followed by intractible ulcer symptoms. Jejunal ulcer demonstrated on Barium meal, 1 year after regastrectomy.

Acid secretion: BAO 9.8 mEq/hr.

MAO 21.2 mEq/hr.

Transabdominal vagotomy performed. Following this, gastric acid secretion dropped to BAO 3.0 mEq/hr., MAO 9.4 mEq/hr.

Follow up: Complete relief of all symptoms 8 months after vagotomy.

Comment:

This patient, a hypersecretor who had had an inadequate resection according to policy of selection, developed a jejunal ulcer 1 year after surgery.

II. E.M. Aet 56.

History: Ulcer dyspepsia for $4\frac{1}{2}$ years. Initially relieved by medical therapy. Acute perforation 5 months prior to surgery, followed by severe dyspepsia not responding to intensive medical therapy.

Investigations: Repeated estimations of gastric acid secretion performed after perforation initially showed:

BAO variation from 70.0 mEq/hr. to 90.0 mEq/hr.

MAO variation from 80.0 mEq/hr. to 118 mEq/hr.

Anticholinergic drugs reduced MAO to 14.2 mEq/hr.

Operation: Standard Polya gastrectomy with vagotomy and amputation of tail of pancreas. The histology of the pancreas failed to reveal any pancreatic lesion.

Post-Operative: Gastric acid secretion was diminished to:

BAO 2.2 mEq/hr.

MAO 12.6 mEq/hr.

Six months later:

BAO 0.0 mEq/hr.

MAO 5.9 mEq/hr.

... Follow

Follow up: Satisfactory.

Comment:

Because of abnormally high BAO:MAO ratio, a Zollinger-Ellison syndrome was very strongly suspected, but because of the marked reduction of the MAO with anticholinergic drugs, a Zollinger-Ellison syndrome was perhaps less likely, and was not found.

III. N.M. Aet 36.

History: 3 year atypical story of intermittent pain in right upper quadrant for 2-3 days associated with increased bowel activity. No definite pain-food relationship. Occasionally had diarrhoea. Two previous laparotomies done in the country for suspected small bowel obstruction. On the second occasion, a mass was found in the head of the pancreas, which was thought to be a Zollinger-Ellison tumour. Subsequently the patient was transferred to Groote Schuur Hospital.

Investigations: Barium meal showed pyloric stenosis.

Acid secretion: BAO 25.5 mEq/hr.
MAO 43.3 mEq/hr.

Operation: Standard Polya gastrectomy with vagotomy. Examination of the pancreas showed no tumour.

Post-Operatively: Augmented histamine test:

BAO 9.3 mEq/hr.
MAO 11.5 mEq/hr.

... Rapid

Rapid increase in weight and free of all pre-operative symptoms 3 years after surgery.

Comment:

Because of high BAO:MAO ratio, a Zollinger-Ellison syndrome was seriously suspected. Post-operative acid output still showed this high ratio. Although a non-beta cell pancreatic tumour could not be demonstrated, and has not manifested itself subsequently, this condition is still suspected and the patient is followed up regularly.

IV. C.M. Aet 65.

History: Two year typical history of ulcer dyspepsia. One episode of haematemesis treated conservatively. No relief with medical therapy. Operation advised because of intractability.

Investigations: Barium meal showed deformed duodenal cap with ulcer crater.

Acid secretion: BAO 11.2 mEq/hr.

MAO 56.3 mEq/hr.

Operation: Standard Polya gastrectomy with vagotomy.

Post-Operatively: Quite well for 14 months following surgery, then started experiencing mild fullness after meals with decrease in the amount of food he was able to take. No other post-gastrectomy symptoms, and no loss of weight, were present.

Acid secretion: BAO 0.0 mEq/hr.

MAO 0.0. mEq/hr.

Barium meal: widely dilated gastric remnant with an obstructed stoma (Fig.XXVI).

... Laparotomy



FIG. XXVI.

Widely dilated gastric remnant with
obstructed stoma - Case Report IV.

Laparotomy: Widely dilated gastric remnant with adhesions, causing stenosis of stoma.

Comment:

Initially a satisfactory result in a patient with a major resection and a vagotomy, presenting over a year later with a major mechanical complication causing the patient only mild discomfort.

V. E.M. Aet 58.

History: Six years history of upper abdominal pain associated with abdominal distension, aggravated by food. Increase in severity of symptoms not responding to medical therapy. Surgery advised because of intractability.

Investigations: Barium meal showed chronic duodenal ulcer.

Augmented histamine test: BAO 7.8 mEq/hr.
MAO 27.0 mEq/hr.

Operation: Gastro-enterostomy with vagotomy.

Post-Operatively: Fourteen months after surgery he experienced post-prandial fullness, associated with retrosternal pain and some difficulty in swallowing.

Acid secretion test: BAO 3 mEq/hr.
MAO 14.2 mEq/hr.

Insulin test: complete vagotomy.

Barium meal: obstruction of second part of duodenum with proximal dilatation (Fig. XXVII).

Laparotomy: Herniation of efferent and afferent loops through transverse mesocolon, causing incomplete obstruction. Posterior gastro-

... enterostomy

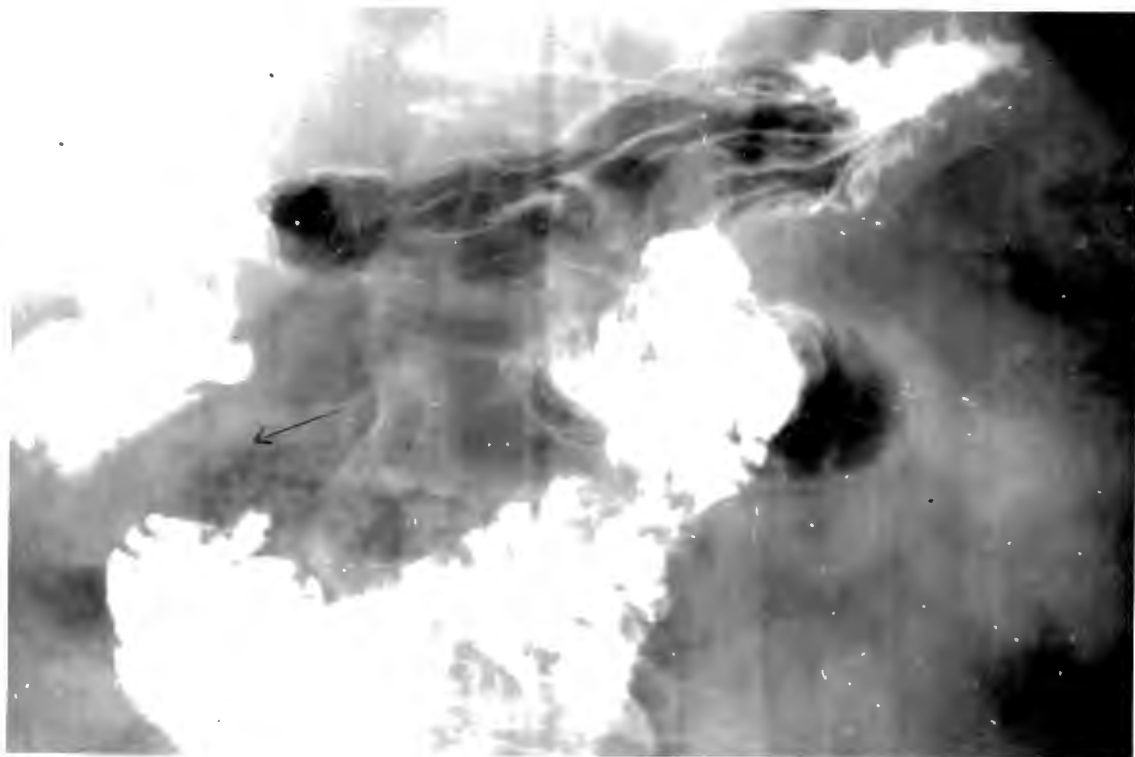


FIG. XXVII.

Herniation of afferent loop through transverse mesocolon with proximal duodenal dilatation following gastroenterostomy with vagotomy - Case Report V.

enterostomy changed to anterior gastro-enterostomy¹

Comment:

An example of an unsatisfactory result in selected group of gastro-enterostomy with vagotomy, due to mechanical factors.

VI. E.F. Aet 77.

History: Intermittent cramp-like pain in left iliac fossa for 4 years, coming on $1\frac{1}{2}$ hours after a meal, relieved by antacids, aggravated by food. For the same period, suffered from intermittent constipation and moderate looseness of stools. Flatulence for 6 months prior to surgery and moderate weight loss for the same period.

Examination: Slight tenderness in left iliac fossa.

Investigations: Occult blood positive. Barium meal showed duodenal scarring.

Acid secretion: BAO 3.0 mEq/hr.
 MAO 20.9 mEq/hr.

Operation: Posterior gastro-enterostomy with vagotomy.

Post-Operatively: One month after surgery she presented with attacks of diarrhoea, loss of appetite, flatulence and audible borborygmi.

Acid secretion: BAO 0.0 mEq/hr.
 MAO 4.2 mEq/hr.

Insulin test: Vagotomy complete.

Radioactive fat excretion: normal.

... Barium

Barium enema showed carcinoma of descending colon. Left hemicolectomy.

Comment:

Unsatisfactory result in a selected case of gastro-enterostomy with vagotomy. Too much significance was attached to an atypical duodenal ulcer story, neglecting to investigate an already existing change in bowel habit. Post-operative diarrhoea could easily have been attributed to vagotomy, unless this symptom was fully followed up and investigated.

VII. E.M. Aet 56.

History: Presented with a 15 year history of burning epigastric pain, not related to meals but relieved by alkalis. Night pain and periodicity marked features. Five years prior to surgery, investigated for duodenal ulceration with negative result. Pain increased and became continuous without complete relief of symptoms on medical therapy. Severe melaena treated medically 3 months before surgery. He also suffered from ischaemic heart disease.

Examination: This showed an emphysematous over-weight individual.

Investigations: Barium meal showed distorted duodenal bulb with moderate dilatation of the stomach.

Acid secretion: BAO 3.8 mEq/hr.
MAO 36.5 mEq/hr.

Standard Polya gastrectomy suggested as procedure of choice.

Operation: At laparotomy a scarred, adherent, oedematous duodenum was found which made it technically dangerous to resect. A gastro-enterostomy with vagotomy was performed.

... Post-

Post-Operatively: Three months after surgery an episode of melaena developed, followed by 3 subsequent melaenas over the next 3 months. Post-prandial pain relieved by alkalis was experienced.

Acid secretion: BAO 7.9 mEq/hr.
MAO 59.2 mEq/hr.

Insulin test: Vagotomy incomplete.

Occult blood: Positive.

Barium meal: no jejunal ulcer could be demonstrated.

Laparotomy: A large jejunal ulcer found. Gastro-enterostomy was changed to a standard Polya gastrectomy.

Comment:

In this patient, with moderate acid secretion, a gastro-enterostomy with an incomplete vagotomy resulted in the early development of jejunal ulceration - an example of the performance of a procedure where success depends on the vagotomy in a patient with too high an acid secretory level, resulting in jejunal ulceration.

VIII E.F. Aet 37.

History: Presented with a 6 year history of periodic ulcer type of dyspepsia. The dyspepsia was characterised by periodic recurrent bouts of epigastric pain and nausea, tending to come on when hungry and relieved by alkalis and anticholinergics.

Investigations: Barium meal 2 years and 1 year before surgery showed an active duodenal ulcer.

Acid secretion: BAO 7.0 mEq/hr.

MAO 26.0 mEq/hr.

Initially, an excellent response to medical treatment was obtained, but her symptoms recurred whilst she was still on treatment. Surgery was advised on grounds of intractability.

Operation: Pyloroplasty with vagotomy.

Post-Operatively: Symptoms recurred 1 month after surgery and continued with slight remissions over the following 8 months. Barium meal performed at this stage was normal, gastroscopy was normal, and the augmented histamine test showed a BAO of 1 mEq/hr. and a MAO of 10 mEq/hr.

... Comment

COMMENT:

Going back into the past history of this patient it appeared that she had led a very sheltered life and was completely unprepared for marriage, finding it difficult to adjust to the sexual demands required of her. Four years after marriage she developed her ulcer dyspepsia. One year after the onset of symptoms she received treatment away from home, with complete relief for 8 months, followed by exacerbation of symptoms, not responding to treatment. Surgery was then performed with recurrence of symptoms 1 month later. She volunteered that she has a good husband, who does not make abnormal demands on her, but finds it difficult to adjust herself sexually and is happier with her symptoms. An example of an unsatisfactory result obtained with a selected procedure in the wrong patient.

IX C.M. Aet 33.

History: Post-prandial pain for 7 years, coming on $\frac{3}{4}$ hour after meals, relieved by food, vomiting and alkalis, followed by symptoms of penetration. Twice had small haematemeses over the 4 years preceding surgery.

Investigations: Barium meal showed no duodenal ulcer.

Acid secretion: BAO 3.9 mEq/hr.
MAO 18.9 mEq/hr.

Operation: Standard Polya gastrectomy.

Post-Operatively: Severe bile vomiting following each meal.

Acid secretion: BAO 0.0 mEq/hr.
MAO 0.1 mEq/hr.

Comment:

A major resection done in a patient with low acid secretion, followed by severe bilious vomiting needing intensive medical treatment. Example of an unnecessary major resection in a low secretor, followed by incapacitating bilious vomiting.

B I B L I O G R A P H Y .

BIBLIOGRAPHY.

A.

ADAM, H.M., CARD, W.I., RIDDELL, M.J., ROBERTS, M., STRONG, S.A. and WOOLF, B.: Dose-response curves for effect of histamine on acid gastric secretion in man. Brit.J.Pharm., 9, 329, 1954.

ANDERSON, C.D., GUNN, R.T.S. and WATT, J.K.: Results of partial gastrectomy in treatment of peptic ulcer. Brit.Med.J., 1, 508, 1955.

ANDERSSON, S.: Inhibitory effects of acid in antrum-duodenum on fasting gastric secretion in Pavlov and Heidenhain pouch dogs. Acta Physiol.Scand., 49, 42, 1960.

ARMSTRONG, R.A. and PENICK, R.M.: The surgical treatment of benign peptic ulcer. Ann.Surg., 152, 109, 1960.

ANTIA, F., ROSIERE, C.E., ROBERTSON, C., and GROSSMAN, M.I.: Effect of vagotomy on gastric secretion and emptying time in dogs. Amer.J.Physiol., 166, 470, 1951.

AUSTEN, W.G. and EDWARDS, H.C.: A clinical appraisal of the treatment of chronic duodenal ulcer by vagotomy and gastric drainage operation. Gut, 2, 158, 1961.

... B

B.

BABKIN, B.P.: Secretory mechanism of the digestive glands. 2nd Ed., Paul B. Hoeber, Inc., 1950.

BACHRACH, W.H.: Laboratory criteria for the completeness of vagotomy. Amer.J.Digest.Dis. (new series), 7, 12, 1962.

BALFOUR, D.C.: Value of co-operation between internist and surgeon in the management of complicated gastric conditions, with some remarks on partial gastrectomy. J.Amer.Med.Ass., 84, 876, 1925.

BANCROFT, F.W.: Modification of Devine operation of pyloric exclusion for duodenal ulcer. Amer.J.Surg., 16, 223, 1932. (Cited by J.O. Robinson: The history of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

BANK, S. and MARKS, I.N.: Personal communication, 1963.

BEAUMONT, W.: Experiments and observations on gastric juice and the physiology of digestion. F.P. Allen, Plattsburg, 1833.

BERGER, E.H.: The distribution of parietal cells in the stomach: a histotopographic study. Amer.J.Anat., 54, 87, 1934.

BIRCHER, E.: Schweiz med.Wschr., 50, 519, 1920 (Cited by J.O. Robinson: The history of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

BLACK, J. and RECHNITZER, P.A.: Haematological and nutritional effects of gastric operations. Quart.J.Med., 22, 419, 1953.

..... BLAIR

BLAIR, E.L., HARPER, A.A. and REED, J.D.: An assay technique for gastrin. J.Physiol., 163, 2 (47 P.), 1962.

BOCKUS, H.L.: Gastroenterology. 2nd Ed. Vol. I, Ch. 23, p.405. W.B. Saunders Co., Philadelphia & London, 1963.

BRAUN, H.: Zbl.Chir., 28, 94, 1899. (Cited by J.O. Robinson: The history of gastric surgery. Postgrad. Med.J., 36, 706, 1960).

BRODIE, B.C.: Experiments and observations on the influences of the nerves of the eight pair on the secretions of the stomach. Phil.Tr.Roy.Soc.London, 104, 102, 1814.

BROOKES, V.S., WATERHOUSE, J.A.H. and THORN, P.A.: Partial gastrectomy for peptic ulcer. Gut, 1, 149, 1960.

BRUCE, J., CARD, W.I., MARKS, I.N. and SIRCUS, W.: The rationale of selective surgery in the treatment of duodenal ulcer. J.Roy.Coll.Surg.Edin., 4, 2, 1959.

BURDENKO, N.: Int.Beitr.Erhahs.Stor., 2, 321, 1914. (Cited by J.O. Robinson: The history of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

BURGE, H.W.: Discussion on the surgical management of chronic duodenal ulcer. Proc.Roy.Soc.Med., 52, 839, 1959.

... BURGE

BURGE, H.W.: Vagotomy in the treatment of peptic ulceration. Postgrad.Med.J., 36, 2, 1960.

BUTLER, T.J.: A study of the pancreatic response to food after gastrectomy in man. Gut, 1, 55, 1960.

C.

CAPPER, W.M. and WELBOURN, R.B.: Early post-cibal symptoms following gastrectomy. Brit.J.Surg., 43, 24, 1955.

CARD, W.I. and BRUCE, J.: Peptic ulcer of the stomach and duodenum. Brit. Surgical Practice (Surgical Progress), p.15. Butterworth & Co., London, 1959.

CARD, W.I. and MARKS, I.N.: The relationship between the acid output of the stomach following "maximal" histamine stimulation and the parietal cell mass. Clin.Sc., 19, 147, 1960.

CARNOT, P., KOSKOWSKI, W. and LIBERT, E.: Action de l'histamine sur la secretion des sucs digestifs chez l'homme. C.R.Soc.Biol. (Paris), 86, 670, 1922.

CARLSON, A.J.: The control of hunger in health and disease. University of Chicago Press, Chicago, 1916.

CHAPMAN, H.N., NYHUS, L.M. and HARKINS, H.N.: The effect of antroneurolysis upon antral function of the stomach. Surg.Gyn.Obstet., 105, 687, 1957.

... CHAPMAN

- CHAPMAN, H.N., NYHUS, L.M. and HARKINS, H.N.: The mechanism of vagus influence on the hormonal phase of gastric acid secretion. *Surgery*, 47, 722, 1960.
- CLARK, C.G., and LOGIE, N.J.: Partial gastrectomy for duodenal ulcer. *J.Roy.Coll.Surg.Edinb.*, 7, 3, 1962.
- CODE, C.F.: The inhibition of gastric secretion: a review. *Pharmacol.Rev.*, 3, 59, 1951.
- CODE, C.F.: Do the vagus nerves have an inhibitory influence on gastric secretion? *Fed.Proc.*, 12, 3, 1953.
- CONARD, V. KOWALEWSKI, K. AND VAN GEERTRUYDEN, J.: Contribution à l'étude de l'achlorhydrie vraie; action de doses croissantes d'histamine sur la secretion gastrique de malades protégés par l'antistine. *Acta Gastroent.Belg.*, 12, 545, 1949.
- CONNELL, F.G.: Fundusectomy: a new principle in the treatment of gastric or duodenal ulcer. *Surg.Gyn.Obstet.* 49, 696, 1929.
- COX, A.J.: Stomach size and its relations to chronic peptic ulcer. *Arch.Path.*, 54, 407, 1952.
- CRILE, G. (Jnr.): An analysis of the vagotomy controversy. *Ann.Surg.*, 136, 752, 1952.

... D

D.

DAVEY, W.: The surgery of anastomotic ulceration.
Ann.Roy.Coll.Surg.Engl., 24, 277, 1959.

DEVINE, H.: Basic principles and supreme difficulties
in gastric surgery. Surg.Gyn.Obstet., 40, 1, 1925.

DE VITO, R.V., JONES, T.W., MARTINIS, A.J., NYHUS, L.M.
and HARKINS, H.N.: Modifications of the gastrin
mechanism by antroneurolysis. Surg.Forum, 9, 423, 1950.

DOLL, R. and JONES, F.A.: Occupational factors in the
aetiology of gastric and duodenal ulcer. Spec.Ref.
Sen.Med.Res.Coun., London, No. 276, 1951.

DRAGSTEDT, L.R. and ELLIS, J.C.: The fatal effects
of total loss of gastric juice. Amer.J.Physiol., 93,
407, 1930.

DRAGSTEDT, L.R., WOODWARD, E.R., STORER, E.H.,
OBERHELMAN, H.R. and SMITH, C.A.: Quantitative studies
of the mechanism of gastric secretion in health and
disease. Ann.Surg., 132, 626, 1950.

DRAGSTEDT, L.R.: Gastric vagotomy in the treatment
of peptic ulcer. Postgrad.Med.J., 10, 482, 1951.

DRAGSTEDT, L.R.: The physiology of gastric secretion
and the peptic ulcer problem. Proc.Mayo Clin., 27,
546, 1952.

DRAGSTEDT, L.R.: The physiology of the gastric antrum.
A.M.A. Arch.Surg., 75, 552, 1957.

... DUVAL

DU VAL, M.K. and PRICE, W.E.: The mechanism of antral regulation of gastric secretion: continuous cross-circulation. Ann.Surg., 152, 410, 1960.

E.

EDKINS, J.S.: The chemical mechanism of gastric secretion. J.Physiol., 34, 133, 1906.

EDWARDS, L.W., HERRINGTON, J.L., CATE, W.R. and LIPSCOMB, A.B.: Gastrojejunal ulcer: problems in surgical management. Ann.Surg., 143, 235, 1956.

EDWARDS, L.W., CLASSEN, K.L. and SAWYERS, J.L.: Experiences and concepts regarding vagotomy and a drainage procedure for duodenal ulcer. Ann.Surg., 151, 827, 1960.

EDWARDS, L.W., EDWARDS, W.H., SAWYERS, J.L., GOBBEL, W.G.(Jnr.), HERRINGTON, J.L. (Jr.) and SCOTT, H.W.: The surgical treatment of duodenal ulcer by vagotomy and antral resection. Amer.J.Surg., 105, 352, 1963.

EVANS, S.O. (Jnr.), ZUBIRAN, J.M., MCCARTHY, J.D. and RAGINS, H., WOODWARD, E.R. and DRAGSTEDT, L.R.: Stimulating effect of vagotomy on gastric secretion in Heidenhain pouch dogs. Amer.J.Physiol., 174, 219, 1953.

EVERSON, T.C. and ALLAN, M.J.: Recurrent or persistent

... peptic

peptic ulceration following secondary operations for peptic ulcer; analysis of 11 cases. Amer.Surgeon, 21, 130, 1955.

EXENER, A.: Dtsch.Z.Chir., 111, 576, 1911. (Cited by J.O. Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

F.

FALCONER, C.W.A.: Discussion on the surgical management of chronic duodenal ulcer. Proc.Roy.Soc. Med., 52, 840, 1959.

FEGETTER, G.Y.: Treatment of chronic duodenal ulcer by vagotomy and posterior gastro-enterostomy. Proc. Roy.Soc.Med., 52, 838, 1959.

FEGETTER, G.Y. and PRINGLE, R.: The long term results of bilateral vagotomy and gastrojejunostomy for chronic duodenal ulcer. Surg.Gyn.Obstet., 116, 175, 1963.

FELDMAN, : Clinical roentgenology of the digestive tract. Williams & Wilkins, 1948.

FENG, T.P., HOU, H.C. and LIM, R.K.S.: On the mechanism of the inhibition of gastric secretion by fat. Chin.J.Physiol., 3, 371, 1929.

FINNEY, J.M.T. (Jnr.): The Finney pyloroplasty. Surg. Gyn.Obstet., 43, 508, 1926.

... FINSTERER

FINSTERER, H.: Anaesthesia in abdominal surgery. Transl. by J.P.F. Burke, Redman and Co., New York, p. 151, 1923. (Cited by J.O. Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

FORREST, A.P.M.: The importance of the innervation of the pyloric antrum in the control of gastric secretion in dogs. Proc. 20th Internat.Physiol.Congress, p.299, 1956.

G.

GELB, M., BARONOFSKY, I.D. and JANOWITZ, H.D.: The effect of vagotomy and pyloroplasty on the maximal acid response to histamine. Gut, 2, 240, 1961.

GILLESPIE, I.E.: Influence of antral pH on gastric acid secretion in man. Gastroent., 37, 164, 1959.

GILLESPIE, I.E., CLARK, D.H., KAY, A.W. and TANKEL, H.I.: Effect of antrectomy, vagotomy and gastro-jejunosomy, and antrectomy with vagotomy, on the spontaneous and maximal gastric acid output in man. Gastroent., 38, 361, 1960.

GILLESPIE, I.E. and KAY, A.W.: Effect of medical and surgical vagotomy on the augmented histamine test in man. Brit.Med.J., 1, 1557, 1961.

GORDON TAYLOR, G.: The present position of surgery in the treatment of bleeding peptic ulcer. Brit.J.Surg., 33, 336, 1946.

... GREGORY

GREGORY, R.A. and IVY, A.C.: The humoral stimulation of gastric secretion. *Quart.J.exp.Physiol.*, 31, 111, 1941.

GREGORY, R.A., TRACY, H.J., FRENCH, J.M. and SIRCUS, W.: The extraction of a gastrin-like substance from a pancreatic tumour in a case of Zollinger-Ellison syndrome. *Lancet*, 1, 1045, 1960.

GRIFFITHS, W.J.: The duodenum and the automatic control of gastric acidity. *J.Physiol.*, 87, 34, 1936.

GRIMSON, K.S.: In discussion of Edwards, L.W., Classen, K.L. and Sawyers, J.L. (1960): Experiences and concepts regarding vagotomy and a drainage procedure for duodenal ulcer. *Ann.Surg.*, 151, 827, 1960.

GROSSMAN, M.I.: Gastro-intestinal hormones. *Physiol. Rev.*, 30, 33, 1950.

GROSSMAN, M.I.: Cholinergic potentiation of the response of gastrin. *J.Physiol.*, 157, 14, 1961.

GROSSMAN, M.I., TRACY, H.J. and GREGORY, R.A.: Zollinger-Ellison syndrome in a Bantu woman, with isolation of a gastrin-like substance from the primary and secondary tumours. II. Extraction of gastrin-like activity from tumours. *Gastroenterol.*, 41, 87, 1961.

... H

H.

HALPERN, B.N.: Recherches sur une nouvelle serie chimique de corps doues de proprietes antihistaminiques et antianaphylactiques: les derives de la thiodiphenylamine. Arch.Int.Pharmacod., 74, 314, 1947.

HARKINS, H.N., JESSEPH, J.E., STEVENSON, J.K. and NYHUS, L.M.: The "combined" operation for peptic ulcer. Arch.Surg., 80, 743, 1960.

HARRISON, R.C., LAKEY, W.H. and HYDE, H.A.: The production of an acid inhibitor by the gastric antrum. Ann.Surg., 144, 441, 1956.

HEINECKE, J.: Inaug.Dissert.Furth., p.13, 1886 (Cited by J.O. Robinson: History of gastric surgery, Postgrad. Med.J., 36, 706, 1960).

HENDRY, W.G.: The treatment of peptic ulceration by vagotomy and Finney pyloroplasty. Postgrad.Med.J., 37, 137, 1961.

HERRINGTON, J.L., EDWARDS, L.W., MCCLASSEN, K.L., CARLSON, R.I., EDWARDS, W.H. and SCOTT, H.W. (Jnr.): Vagotomy and antral resection in the treatment of duodenal ulcer: Results in 514 patients. Ann.Surg., 150, 499, 1959.

HERRINGTON, J.L.: Selecting the operation for the particular patient in cases of duodenal ulcer. Surgery, 47, 497, 1960.

HERTZ, A.F.: The cause and treatment of certain unfavourable after-effects of gastro-enterostomy. Ann.Surg., 58, 466, 1913.

... HIRSCHOWITZ

HIRSCHOWITZ, B.I., POLLARD, H.M., HARTWELL, S.W. and LONDON, J.: The action of ethyl alcohol on gastric acid secretion. Gastroent., 30, 244, 1956.

HOERR, S.O.: Duodenal ulcer treated by subdiaphragmatic vagus resection and posterior gastro-enterostomy: interim report. Arch.Surg., 67, 436, 1953.

HOERR, S.O.: Elective operations performed for duodenal ulcer, with their mortality. Amer.J.Surg., 96, 365, 1958.

HOERR, S.O.: Surgery of chronic duodenal ulcer: comparison of results with vagotomy - posterior gastro-jejunosomy and with vagotomy - hemigastrectomy: evaluation of a personal series of 200 patients. Cleveland Clin.Quart., 26, 1170, 1959.

HOLLANDER, F.L: The Insulin test for the presence of intact nerve fibres after vagal operations for peptic ulcer. Gastroent., 7, 607, 1946.

HOLLANDER, F.: Laboratory procedures in the study of vagotomy (with particular reference to the insulin test). Gastroent., 11, 419, 1948.

HOLT, R.L.: Discussion on the surgical management of chronic duodenal ulcer. Proc.Roy.Soc.Med., 52, 837, 1959.

HOLT, R.L. and LYTHGOE, J.P.: Ten year results of vagotomy and gastrojejunostomy in the treatment of chronic duodenal ulcer. Brit.J.Surg., 215, 255, 1961.

... HUNT

HUNT, J.N.: The investigation of gastric digestive function in man. Lect.Sci.Basis Med., 5, 348, 1956.

HUNT, J.N. and KAY, A.W.: The nature of gastric hypersecretion of acids in patients with duodenal ulcer. Brit.Med.J., ii, 1444, 1959.

HURST, A.F. and STEWART, M.J.: Gastric and duodenal ulcer. pp. 29, 97. Oxford Univ.Press Medical Publications, London, 1929.

I.

IVY, A.C. and FARRELL, J.I.: Contributions to the physiology of gastric secretion. VIII. The proof of a humoral mechanism. Amer.J.Physiol., 74, 639, 1925.

IVY, A.C., GROSSMAN, M.I. and BACHRACH, W.H.: Peptic ulcer. Blakiston, Philadelphia. 1950.

... J.

J.

- JONES, T.W., DE VITO, R.V., NYHUS, L.M. and HARKINS, H.N.: The effect of antroneurolysis upon antral function of the stomach. Surg.Gyn.Obstet., 105, 687, 1957.
- JONES, T.W. and HARKINS, H.N.: The mechanism of inhibition of gastric acid secretion by the duodenum. Gastroent., 37, 81, 1959.
- JONES, Avery F. and GUMMER, J.W.P.: Clinical Gastroenterology. Blackwell Scientific Publications, Oxford, 1961.
- JOHNSON, H.D. and ORR, I.M.: Selective surgery for peptic ulcer. Surg.Gyn.Obstet., 98, 425, 1954.
- JOHNSON, H.D.: The classification and principles of treatment of gastric ulcers. Lancet, 273, 518, 1957.
- JOHNSON, H.D.: Surgical aspects of medicine. (Editor). Butterworth, London, 1959.
- JOHNSON, A.N. (Jnr.), COBO, A. OBERHELMAN, H.A.(Jnr.), and DRAGSTEDT, L.R.: Inhibition of acid secretion by acid in the antrum. Surg.Forum, 10, 155, 1960.
- JORDAN, P.H. (Jnr.) and SAND, B.F.: Antral inhibition of gastric secretion. Proc.Soc.exp.Biol.Med., 94, 471, 1957.

K.

- KANAR, E.A., SCHMITZ, E.J., SAUVAGE, L.R., STORER, E.H. and HARKINS, H.N: The secretory response of the stomach to gastro-enterostomy, as measured by a Heidenhain pouch. Surg.Forum, 3, 12, 1952.
- KAY, A.W.: Effect of large doses of histamine on gastric secretion of HCl - an augmented histamine test. Brit. Med.J., 2, 77, 1953.

... KAY

KAY, A.W.: Gastro-intestinal surgery and human physiology. Honyman: Gillespie Lecture, 1961.

KOMAROV, S.A.: Gastrin. Proc.Soc.exp.Biol., 38, 514, 1938.

L.

LATARJET, A.: Bull.acad.Med. 87, 681, 1922. (Cited by J.O. Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

LEES, F. and GRANDJEAN, L.C.: The gastric and jejunal mucosa in healthy patients with partial gastrectomy. Arch.intern.Med., 101, 943, 1958.

LEVIN, E., KIRSNER, J.B. and PALMER, W.L.: The nocturnal gastric secretion in patients with gastric carcinoma; a comparison with normal individuals and patients with duodenal ulcer and with gastric ulcer. Gastroent., 12, 56, 1949.

LEVIN, E., KIRSNER, J.B. and PALMER, W.L.: Differences in gastric secretion in normal individuals and patients with peptic ulcer; their bearing on ulcer management. Rev.Gastroent., 19, 226, 1952.

LIM, R.K.S., IVY, A.C. and McCARTHY, J.E.: Contributions to the physiology of gastric secretion. I. Gastric secretion by local (mechanical and chemical)

... stimulation

stimulation. Quart.J.exp.Physiol., 15, 13, 1925.

LIM, R.K.S. and MOZER, P.: Mechanism of excitation of internal secretion of pylorus and adenteric reflex. Amer.J.Physiol., 163, 730, 1958.

LIM, R.K.S. and MOZER, P.: Does vagus excitation liberate pyloric gastrin? Fed.Proc., 10, 81, 1951.

LINDERSTRØM-LANG, K., HOLTER, H. and SØEBERG OHLSON, A.: Beitrage zur enzymatischen histochemie. XIII. Die enzymverteilung im Schweinemagen als funktion zeines histologischen aufbaus. Arch.Pharm.Chemi, 227, 1, 1934.

LONGHI, E.H., GREENLEE, H.B., BRAVO, J.L., GUERRERO, J.D. and DRAGSTEDT, L.R.: Question of an inhibitory hormone from gastric antrum. Amer.J.Physiol., 191, 64, 1957.

LUFF, A.P.: The after-history of gastro-enterostomy. Brit.Med.J., 2, 1074, 1929.

M.

MARKS, I.N.: The significance of the gastric secretion after partial gastrectomy and gastro-enterostomy. Amer.J.Gastroent., 27, 566, 1957.

MARKS, I.N. and SHAY, H.: Unpublished data, 1959.

MARKS, I.N. and SHAY, H.: Observations on the pathogenesis of gastric ulcer. Lancet, 276, 7083, 1109, 1959.

... MARKS

MARKS, I.N., KOMAROV, S.A. and SHAY, H.: Maximal acid secretory response to histamine and its relationship to parietal cell mass in the dog. Amer. J.Physiol., 199, 579, 1960.

MARKS, I.N., SELZER, G., LOUW, J.H. and BANK, S.: Zollinger-Ellison syndrome in a Bantu woman, with isolation of a gastrin-like substance from the primary and secondary tumours. I. Case Report. Gastroent., 41, 77, 1961.

MARKS, I.N.: Editorial. Gastroent., 41, 599, 1961.

MARKS, I.N., and BANK, S.: Personal communication, 1963.

MEYERS, W.C.: Study of gastric mucosa in various diseases affecting the upper part of the gastrointestinal tract. Gastroent., 10, 923, 1948.

MOYNIHAN, B.G.A.: Abdominal operations. W.B. Saunders & Co., Philadelphia, 1928.

MUNCH-PETERSEN, J., RÖNNOW, G. and UVNÄS, B.: Further studies on the gastric secretory excitant from the pyloric mucosa. Acta Physiol.Scand., 7, 289, 1944.

MUIR, A.: Post-gastrectomy syndromes. Brit.J.Surg., 37, 165, 1949.

MURRAY, F.A., ERSKINE, J.P. and FIELDING, J.: Gastric secretion in pregnancy. J.Obstet.Gynaec.Brit.Emp., 64, 373, 1957.

N.

NYHUS, L.M., CHAPMAN, N.D., DE VITO, R.V. and HARKINS, H.N.: The control of gastrin release: an experimental study illustrating a new concept. Gastroent., 39, 582, 1960.

O.

OBERHELMAN, H.A. (Jnr.), RIGLER, S.P. and DRAGSTEDT, L.R.: The significance of innervation in the function of the antrum. Amer.J.Physiol., 190, 391, 1957.

ORR, I.M.: Selective surgery for peptic ulcer: a review. Gut, 3, 97, 1962.

ORR, I.M.: Selective surgery for peptic ulcer. Brit.J.Surg., 220, 121, 1962.

ORR, I.M.: Selective surgery for peptic ulcer. J.Roy.Coll.Surg.Edinb., 8, 277, 1963.

P.

PALUMBO, L.T. and SHARPE, W.S.: Partial gastrectomy for chronic duodenal ulcer: results of follow up in 700 cases. Surgery, 48, 658, 1960.

PALUMBO, L.T., LULU, D.J., VESPA, R. and COHEN-BONET, J.: Antrectomy with vagectomy or partial gastrectomy with or without vagectomy for chronic duodenal ulcer: a comparative analysis. Ann.Surg., 151, 367, 1960.

... PAVLOV

PAVLOV, I.P.: The work of the digestive glands.
Chas.Griffin & Co. Ltd., London, 1902.

PETERSEN, W.: Beitr.Klin.Chir., 29, 597, 1901. (Cited
by J.O. Robinson: History of gastric surgery. Postgrad.
Med.J., 36, 706, 1960).

PINCUS, I.J., THOMAS, J.E. and REHFUSS, M.D.: A study
of gastric secretion as influenced by changes in
duodenal acidity. Proc.Soc.exper.Biol.Med., 51, 367,
1942.

POLLOCK, A.V.: Vagotomy in the treatment of peptic
ulceration. Review of 1524 cases. Lancet, 2, 795, 1952.

POPIELSKI, L.B.; β -Imidazolyläthylamia und die
organextrakte. I. B-Imidazolaläthylamia als mächtiger
Erreger der Magendrösen. Pflüger Arch.Ges.Physiol.,
178, 214, 1920.

PRIESTLEY, J.T. and GIBSON, R.H.: Gastro-duodenal ulcer:
clinical features and late results. Arch.Surg., 56,
625, 1948.

PROUT, W.: On the nature of the acid and saline matters
usually existing in the stomach of animals. Philosoph.
Trans.Royal Soc., London. Part I., p.45, 1824.

PULVERTAFT, C.N.: The results of partial gastrectomy
for peptic ulcer. Lancet, 1, 225, 1952.

... R

R.

ROSCOE GRAHAM, R.: Technical surgical procedures for gastric and duodenal ulcer. Surg.Gyn.Obstet., 66, 269, 1938.

ROTH, J.L.A. and BOCKUS, H.L.: Why do a gastric analysis? Gastroent., 18, 546, 1951.

ROUX, J.C.: Rev.Gynae. 1, 67, 1897. (Cited by J.O.Robinson: History of gastric surgery. Postgrad. Med.J., 36, 706, 1960).

S.

SANDWEISS, D.J., BARBORKA, C.J., BOCKUS, H.L., IVY, A.C., JORDAN, S.M., MILLER, T.G., PALMER, W.L., WANGENSTEEN, O.H., RUFFIN, J.M., AARON, A.H., HOLLANDER, F., THOMAS, J.E., WALTERS, W., MOORE, F.D., WINKELSTEIN, A., BROOKS, F.P. and LORGE, I.: Report of the Committee on Surgical Procedures of the National Committee on Peptic Ulcer of the American Gastroenterological Assoc. on study of vagotomy, study of gastric resection, comparative study of vagotomy and gastric resection. Gastroent., 22, 295, 1952.

SCHOEMAKER, J. Arch.Klin.Chir., 94, 541, 1911. (Cited by J.O. Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

SCHNUG, G.E. and CAVANAGH, C.R.: An analysis of morbidity and mortality following gastric surgery for ulcer. Amer.J.Surg., 104, 224, 1962.

... SCOTT

SCOTT, H.W., HERRINGTON, J.L., EDWARDS, L.W., SKELL, H.J., STEPHENSON, S.E., SAWYERS, J.L. and CLASSEN, K.L.: Results of vagotomy and antral resection in surgical treatment of duodenal ulcer. Gastroent., 39, 350, 1960.

SCHWANN, T. quoted by PORTIS. Diseases of the Digestive System. Lea and Febiger, Philadelphia, p.33. 1944.

SHAPIRA, D., MORGENSTERN, L. and STATE, D.: Critical examination of "acid-inhibition" phenomenon in dogs with twin antrum pouches. Surg.Forum, 10, 143, 1960.

SHAY, H., GERSHON-COHEN, J. and FELS, S.S.: A self-regulatory duodenal mechanism for gastric acid control and an explanation for the pathologic gastric physiology in uncomplicated duodenal ulcer. Amer.J.Digest.Dis. 9, 124, 1942.

SHAY, H.: Emotional stress and the parietal cell mass. Amer.J.Digest.Dise., 4, 486, 1959.

SHERREN, J.: Gastro-jejunostomy (Bradshaw Lecture). Lancet, 2, 1007, 1925.

SIRCUS, W.: The intestinal phase of gastric secretion. Quart.J.exp.Physiol., 38, 91, 1953.

SIRCUS, W.: Studies on the mechanisms in the duodenum inhibiting gastric secretion. Quart.J.exper.Physiol., 43, 114, 1958.

SIRCUS, W.: The application of the "maximal" histamine test of gastric secretion to problems of peptic ulcer surgery. J.Roy.Coll.Surg.Edinb., 4, 153, 1959.

... SIRCUS

SIRCUS, W.: The surgery of peptic ulcers, in Peptic Ulceration - a Symposium for Surgeons. Ed. C. Wells and J. Kyle. The Williams & Wilkins Co., Baltimore, 1960.

SMITH, A.N. and KAY, A.W.: The action of atropine and hexamethonium in combination on gastric secretion and motility. Brit.J.Pharmacol., 2, 331, 1956.

SMITH, G.K., and FARRIS, J.M.: Vagotomy and pyloroplasty in chronic duodenal ulcer with special reference to technique. Arch.Surg., 78, 652, 1959.

SMITHWICK, R.H.: Conservative gastric resection combined with vagotomy. Surgery, 41, 344, 1957.

SMITHWICK, R.H., HARROWER, H.W. and FARMER, D.A.: Hemigastrectomy and vagotomy in the treatment of duodenal ulcer. Amer.J.Surg., 101, 325, 1961.

SOKOLOV, A.P. Cited by Babcock, B.P. Secretory mechanism of the Digestive Glands. Paul Hoeber Inc., New York, 1950.

STAMMERS, F.A.R.: Mechanical factors as a cause for gastrectomy failures. J.Roy.Coll.Surg.Edinb., 4, 121, 1959.

STAVNEY, L.S., KATO, D., CHAPMAN, N.D., NYHUS, L.M. and HARKINS, H.N.H. - Unpublished observations. Quoted by Nyhus, L.M., Condon, R.E. and Harkins, H.N.: The evolution of surgery for duodenal ulcer during the mid-twentieth century. J.Roy.Coll.Surg.Edinb., 8, 94, 1962.

... STEIN

STEIN, I.F., MEYER, K.A.: Studies of vagotomy in treatment of peptic ulcer. Surg.Gyn.Obstet., 86, 473, 1948.

STEMPIEN, S.J., FRENCH, J.D., DAGRADI, A. MOVIUS, H.J. and PORTER, R.W.: The early and delayed phases of gastric acid secretion in response to insulin hypoglycaemia. Gastroent., 34, 111, 1958.

STEMPIEN, S.J., DAGRADI, A.E., SEIFER, H.W.: Status of duodenal ulcer patients 5 years or more after vagotomy - pyloroplasty. Proc. World Congress of Gastroenterology, p.1026. Williams & Wilkins Co., Baltimore, 1958.

STEVENS, F.O. and KYLE, J.: Gastric acidity after duodenal ulcer surgery. J.Surg.Research, 3, 29, 1963.

STRATTEN, T.: Die Bedeutung der Pylorus drüsenzzone für die Magensekretion. Arch.Klin.Chir., 175, 236, 1933.

STUMPF, R.: Beitr.Klin.Chir., 59, 551, 1908. (Cited by J.O. Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960.

T.

TANNER, N.C.: Indications for surgery in peptic ulcer. Edinb.Med.J., 58, 261, 1951.

... TANNER

TANNER, N.C.: Surgery of peptic ulceration and its complications. (Lettsomian Lecture). Postgrad.Med.J., 30, 448, 1954.

TANNER, N.C.: Discussion on the surgical management of chronic duodenal ulcer. Proc.Roy.Soc.Med., 52, 840, 1959.

TANNER, N.: Present views on the surgery of the stomach and duodenum. J.Roy.Coll.Surg.Edin., 8, 4, 1963.

THEIN, M.P. and SCHOFIELD, B.: Release of gastrin from the pyloric antrum following vagal stimulation by sham feeding in dogs. J.Phys., 145, 14, 1958.

THOMPSON, J.E.: Stomal ulceration after gastric surgery. Ann.Surg., 143, 697, 1956.

THOMPSON, J.C. and LERNER, H.J.: Demonstration of antral inhibitory hormone by cross transfusion. J.Surg.Research, 1, 117, 1961.

TONGEN, L.A.: The qualitative relationship between parietal cells and gastric acidity. Surgery, 28, 1009, 1950.

U.

UVNÄS, B.: The part played by the pyloric region in the cephalic phase of gastric secretion. Acta Phys.Scand., 4, Suppl. 13, 1942.

V.

VISICK, A.H.: Measured radical gastrectomy. A review of 505 operations. Lancet, 1, 505 and 551, 1948.

... VON

VON HACKER, V.: Verh.Dtsch.ges.Chir., 1, 74, 1885.

(Cited by J.O. Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

VON MIKULICZ-RADECKI, J.: Arch.Klin.Chir., 37, 79, 1888.

(Cited by J.O.Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

VON RYDYGIER, L.: Przegl.lek., 19, 637, 1880. (Cited by J.O. Robinson: History of gastric surgery. Postgrad. Med.J., 36, 706, 1960).

W.

WADDELL, W.R.: The acid response to histamine and insulin hypoglycaemia after various operations on the stomach. Surgery, 47, 652, 1957.

WALTERS, W., CHANCE, D.P. and BERKSON, J.: A comparison of vagotomy and gastric resection for gastro-jejunal ulceration - a follow up of 301 cases. Surg.Gyn.Obstet., 100, 1, 1955.

WALTERS, W., THOMAS, E.L. and MOBLEY, J.E.: A 5 to 10 year follow up study of the Bilroth I and Bilroth II (Polya) operations for duodenal, gastric and gastro-jejunal ulcer and gastro-enterostomy with vagotomy in the treatment of duodenal ulcer. Gastroent., 33, 685, 1957.

WANGENSTEEN, O.H., VARCO, R.L., HAY, L., WALPOLE, S. and TRACH, B.: Gastric acidity before and after operative procedure, with special reference to the role of the pylorus and antrum: preliminary report of clinical and experimental study. Ann.Surg., 112, 626, 1940.

... WANGENSTEEN.

WANGENSTEEN, O.H.: Aseptic gastric resection. I. A method of aseptic anastomosis adaptable to any segment of the alimentary canal (esophagus, stomach, small or large intestine). II. Including preliminary description of subtotal excision. Surg.Gyn.Obstet., 70, 59, 1940.

WANGENSTEEN, O.H.: Segmental gastric resection for peptic ulcer. J.Amer.Med.Ass., 149, 18, 1952.

WEINBERG, J.A.: Vagotomy with pyloroplasty in treatment of duodenal ulcer - surgical aspects. Amer.J.Gastroent., 21, 296, 1954.

WEINBERG, J.A.: Vagotomy and pyloroplasty in the treatment of duodenal ulcer. Amer.J.Surg., 105, 347, 1963.

WELCH, C.E.: The treatment of acute, massive gastroduodenal haemorrhage. J.Amer.Med.Assoc., 141, 1113, 1949.

WELCH, C.E. and RODKEY, G.V.: Partial gastrectomy for duodenal ulcer. Amer.J.Surg., 105, 338, 1963.

WELBOURN, R.B., and JOHNSTON, I.D.A.: The assessment and selection of elective operations for peptic ulceration. British Surg. Practice (Surgical Progress) Butterworth, London. P.305. 1961.

WELLS, C.A. and MacPHEE, I.W.: Partial gastrectomy: Ten years later. Brit.Med.J., 2, 1128, 1954.

... WILKIE

WILKIE, D.P.D.: Coincident duodenal and gastric ulcer. Brit.Med.J., 2, 469, 1926.

WINKELSTEIN, A.: Some observations on the relationship of vagus nerve to peptic ulcer. J.Mount Sinai Hosp., N.Y., 9, 859, 1942.

WOELFLER, A. : Wien Med.Wschr., 31, 1427, 1881.
(Cited by J.O. Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

WOELFLER, A.: Verh.dtsch.ges.Chir., 12, 22, 1883.
(Cited by J.O. Robinson: History of gastric surgery. Postgrad.Med.J., 36, 706, 1960).

WOLF, J., ROSSMAN, M. and FLOOD, C.F.: Gastrosopic findings in patients with subtotal gastrectomy. Gastroent., 32, 1050, 1957.

WOODWARD, E.R., LYONS, E.S., LANDOR, J.A. and DRAGSTEDT, L.R.: The physiology of the gastric antrum; experimental studies on isolated antrum pouches in dogs. Gastroent., 27, 766, 1954.

WOODWARD, E.R., ROBERTSON, C., FRIED, W. and SHAPIRO, H.: Further studies on the isolated gastric antrum. Gastroent., 32, 868, 1957.

WOODWARD, E.R., TRUMBULL, W.E., SHAPIRO, H. and TOWNE, L.: Does the gastric antrum elaborate an antiseecretory hormone? Amer.J.Digest.Dis., 3, 204, 1958.

WOROBJEW, A.M. and VOLVORTH, G.W.: The significance of the pyloric part of the stomach in the activity of the gastric glands. J.Physiol., U.S.S.R., 17, 1281, 1934.

XYZ

ZUBIRAN, J.M., KARK, A.E., MONTALBETTI, A., MOREL, C.J.L. and DRAGSTEDT, L.R.: Quantitative studies on the effect of gastrojejunostomy on gastric secretion. Arch.Surg., 65, 239, 1952.

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